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(54) **(R)-CHIRAL HALOGENATED 1-SUBSTITUTEDAMINO-(N+1)-ALKANOLS USEFUL FOR INHIBITING CHOLESTERYL ESTER TRANSFER PROTEIN ACTIVITY**

(R)-CHIRALE HALOGENIERTE 1-SUBSTITUIERTE AMINO-(N+1)-ALKANOLEN FÜR DIE HEMMUNG DER AKTIVITÄT DES CHOLESTERYL-ESTER-TRANSFER-PROTEINS

AMINO-(N+1)-ALCANOLS 1-SUBSTITUES HALOGENES R-CHIRAUX, UTILES COMME INHIBITEURS DE L'ACTIVITE DE LA PROTEINE DE TRANSFERT DE L'ESTER DE CHOLESTERYLE

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Description

FIELD OF THE INVENTION

[0001] This invention is in the field of treating cardiovascular disease, and specifically relates to compounds and compositions for treating atherosclerosis and other coronary artery disease, and methods for making compounds of this invention. More particularly, the invention relates to (R)-chiral halogenated 1-substitutedamino-(n+1)-alkanol compounds that inhibit cholesteryl ester transfer protein (CETP), also known as plasma lipid transfer protein-I.

BACKGROUND OF THE INVENTION

[0002] Numerous studies have demonstrated that a low plasma concentration of high density lipoprotein (HDL) cholesterol is a powerful risk factor for the development of atherosclerosis (Barter and Rye, *Atherosclerosis*, 121, 1-12 (1996)). HDL is one of the major classes of lipoproteins that function in the transport of lipids through the blood. The major lipids found associated with HDL include cholesterol, cholesteryl ester, triglycerides, phospholipids and fatty acids. The other classes of lipoproteins found in the blood are low density lipoprotein (LDL) and very low density lipoprotein (VLDL). Since low levels of HDL cholesterol increase the risk of atherosclerosis, methods for elevating plasma HDL cholesterol would be therapeutically beneficial for the treatment of atherosclerosis and other diseases associated with accumulation of lipid in the blood vessels. These diseases include, but are not limited to, coronary heart disease, peripheral vascular disease, and stroke.

[0003] Atherosclerosis underlies most coronary artery disease (CAD), a major cause of morbidity and mortality in modern society. High LDL cholesterol (above 180 mg/dl) and low HDL cholesterol (below 35 mg/dl) have been shown to be important contributors to the development of atherosclerosis. Other diseases, such as peripheral vascular disease, stroke, and hypercholesterolaemia are negatively affected by adverse HDL/LDL ratios. Inhibition of CETP by the subject compounds is shown to effectively modify plasma HDL/LDL ratios, and to check the progress and/or formation of these diseases.

[0004] CETP is a plasma protein that facilitates the movement of cholesteryl esters and triglycerides between the various lipoproteins in the blood (Tall, *J. Lipid Res.*, 34, 1255-74 (1993)). The movement of cholesteryl ester from HDL to LDL by CETP has the effect of lowering HDL cholesterol. It therefore follows that inhibition of CETP should lead to elevation of plasma HDL cholesterol and lowering of plasma LDL cholesterol, thereby providing a therapeutically beneficial plasma lipid profile (McCarthy, *Medicinal Res. Revs.*, 13, 139-59 (1993); Sitori, *Pharmac. Ther.;* 67,443-47 (1995)). This exact phenomenon was first demonstrated by Swenson et al., (*J. Biol. Chem.*, 264, 14318 (1989)) with the use of a monoclonal antibody that specifically inhibited CETP. In rabbits, the antibody caused an elevation of the plasma HDL cholesterol and a decrease in LDL cholesterol. Son et al. *(Biochim. Biophys. Acta* 795, 743-480 (1984)), Morton et al. *(J. Lipid Res.* 35, 836-847 (1994)) and Tollefson et al. *(Am. J. Physiol.,* 255, (Endocrinol. Metab. 18, E894-E902 (1988))) describe proteins from human plasma that inhibit CETP. U.S. Patent 5,519,001, issued to Kushwaha et al., describes a 36 amino acid peptide derived from baboon apo C-1 that inhibits CETP activity. Cho et al. *(Biochim. Biophys. Acta* 1391, 133-144 (1998)) describe a peptide from hog plasma that inhibits human CETP. Bonin et al. (*J. Peptide Res.*, 51, 216-225 (1998)) disclose a decapeptide inhibitor of CETP. A depsipeptide fungal metabolite is disclosed as a CETP inhibitor by Hedge et al. in *Bioorg. Med. Chem. Lett.*, 8, 1277-80 (1998).

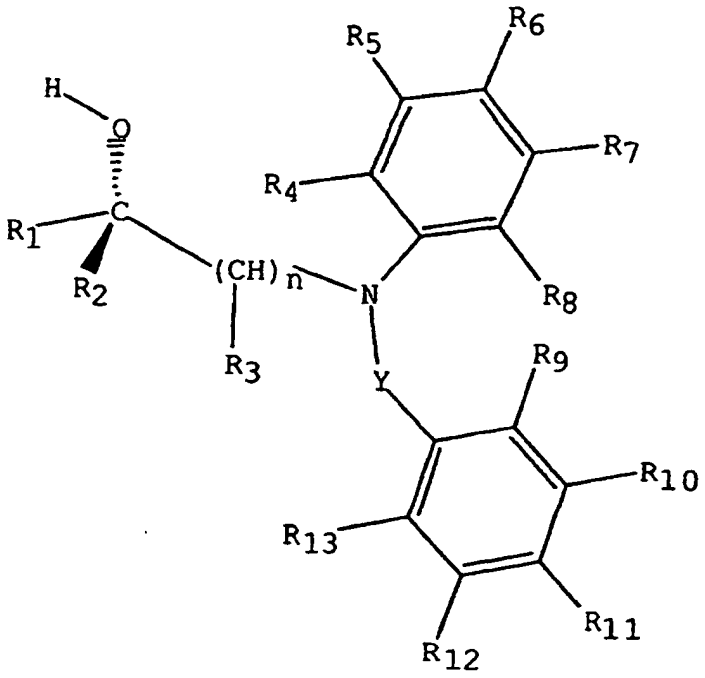
[0005] There have been several reports of non-peptidic compounds that act as CETP inhibitors. Barrett et al. *(J. Am. Chem. Soc.*, 188, 7863-63 (1996)) and Kuo et al. *(J. Am. Chem. Soc.*, 117, 10629-34 (1995)) describe cyclopropane-containing CETP inhibitors. Pietzonka et al. *(Bioorg. Med. Chem. Lett*, 6, 1951-54 (1996)) describe phosphonate-containing analogs of cholesteryl ester as CETP inhibitors. Coval et al. (*Bioorg. Med. Chem. Lett.*, 5, 605-610 (1995)) describe Wiedendiol-A and -B, and related sesquiterpene compounds as CETP inhibitors. Japanese Patent Application No. 10287662-A describes polycyclic, non-amine containing, polyhydroxylic natural compounds possessing CETP inhibition properties. Lee et al. (*J. Antibiotics*, 49, 693-96 (1996)) describe CETP inhibitors derived from an insect fungus. Busch et al. *(Lipids,* 25, 216-220, (1990)) describe cholesteryl acetyl bromide as a CETP inhibitor. Morton and Zilversmit (*J. Lipid Res.*, 35, 836-47 (1982)) describe that p-chloromercuriphenyl sulfonate, p-hydroxymercuribenzoate and ethyl mercurithiosalicylate inhibit CETP. Connolly et al. (*Biochem. Biophys. Res. Comm.* 223, 42-47 (1996)) describe other cysteine modification reagents as CETP inhibitors. Xia et al. describe 1,3,5-triazines as CETP inhibitors (Bioorg. Med. Chem. Lett., 6, 919-22 (1996)). Bisgaier et al. (*Lipids,* 29, 811-8 (1994)) describe 4-phenyl-5-tridecyl-4H-1,2,4-triazole-thiol as a CETP inhibitor. Oomura et al. disclose non-peptidic tetracyclic and hexacyclic phenols as CETP inhibitors in Japanese Patent Application No. 10287662.

[0006] Some substituted heteroalkylamine compounds are known. In European Patent Application No. 796846, Schmidt et al. describe 2-aryl-substituted pyridines as cholesteryl ester transfer protein inhibitors useful as cardiovascular agents. One substituted at C3 of the pyridine ring can be an hydroxyalkyl group. In European Patent Application No. 801060, Dow and Wright describe heterocyclic derivatives substituted with an aldehyde addition product of an

alkylamine to afford 1-hydroxy-1-amines. These are reported to be β3-adrenergic receptor agonists useful for treating diabetes and other disorders. In Great Britain Patent Application No. 2305665, Fisher et al. disclose 3-agonist secondary amino alcohol substituted pyridine derivatives useful for treating several disorders including cholesterol levels and artherosclerotic diseases. In European Patent Application No. 818448, Schmidt et al. describe tetrahydroquinoline derivatives as cholesteryl ester transfer protein inhibitors. European Patent Application No. 818197, Schmek et al. describe pyridines with fused heterocycles as cholesteryl ester transfer protein inhibitors. Brandes et al. in German Patent Application No. 19627430 describe bicyclic condensed pyridine derivatives as cholesteryl ester transfer protein inhibitors. In WO Patent Application No. 09839299, Muller-Gliemann et al. describe quinoline derivatives as cholesteryl ester transfer protein inhibitors. U.S. Patent 2,700,686, issued to Dickey and Towne, describes N-(2-haloalkyl-2-hydroxyethyl)amines in which the amine is further substituted with either 1 to 2 aliphatic groups or one aromatic group and one aliphatic group. U.S. Patent 2,700,686 further describes a process to prepare the N-(2-haloalkyl-2-hydroxyethyl)amines by reacting halogenated-1,2-epoxyalkanes with the corresponding aliphatic amines and N-alkylanilines and their use as dye intermediates.

SUMMARY OF THE INVENTION

[0007] The present invention provides chiral compounds that can be used to inhibit cholesteryl ester transfer protein (CETP) activity and that have the general structure:

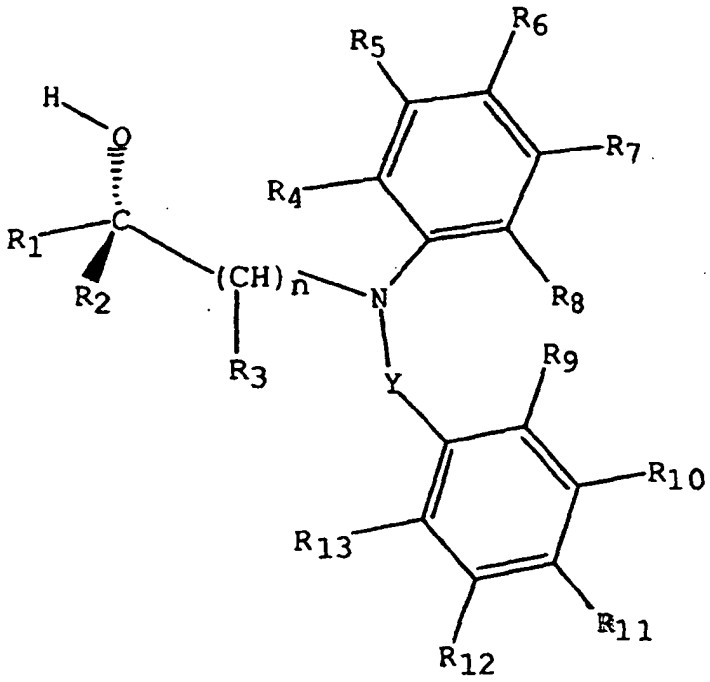


[0008] In another aspect, the present invention includes pharmaceutical compositions comprising a pharmaceutically effective amount of the chiral compounds of this invention and a pharmaceutically acceptable carrier.

[0009] In another aspect, this invention relates to, but does not claim as such, methods of using these chiral inhibitors as therapeutic agents in humans to inhibit cholesteryl ester transfer protein (CETP) activity, thereby decreasing the concentrations of low density lipoprotein (LDL) and raising the level of high density lipoprotein (HDL), resulting in a therapeutically beneficial plasma lipid profile. The compounds and methods of this invention can also be used to treat dyslipidemia (hypoalphalipoproteinemia), hyperlipoproteinaemia (chylomicronemia and hyperapobetalipoproteinemia), peripheral vascular disease, hypercholesterolaemia, atherosclerosis, coronary artery disease and other CETP-mediated disorders. The compounds can also be used in prophylactic treatment of subjects who are at risk of developing such disorders. The compounds can be used to lower the risk of atherosclerosis. The compounds of this invention would be also useful in prevention of cerebral vascular accident (CVA) or stroke. Besides being useful for human treatment, these compounds are also useful for veterinary treatment of companion animals, exotic animals and farm animals such as primates, rabbits, pigs, horses, and the like.

DESCRIPTION OF THE INVENTION

[0010] The present invention relates to a class of compounds comprising (R)-chiral halogenated 1-substitutedamino-(n+1)-alkanols which are beneficial in the therapeutic and prophylactic treatment of coronary artery disease as given in the following Formula M:



or a pharmaceutically acceptable salt thereof, wherein;

n is selected from the integers 1, 2, 3 and 4;

Y is $-(CH_2)_q-$ wherein q is 1 or 2;

R_1 is haloalkyl;

R_2 is hydrido;

R_3 is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride, halo, haloalkyl, and alkyl;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, C1-C6 alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylamidosulfonyl, arylsulfonamido, alkylarylamidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, C3-C7 cycloalkylalkyl, C3-C7 cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, heteroaralkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cyano, cycloalkoxy,

cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl, haloalkylthio, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, halocycloalkyl, halocycloalkenyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxy, hydroxy, thio, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, arylsulfonyl, alkenoyl, aroyl, aralkanoyl, haloalkanoyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, cycloalkylalkanoyl, C3-C7 cycloalkylalkyl, haloalkenyl, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, carboxyalkyl, carboalkoxy, alkoxycarbonyl, carboaralkoxy, carboxamido, carboxamidoalkyl, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl,

with the proviso that at least one of R_4, R_5, R_6, R_7, and R_8 is not hydrido,

and with the further proviso that at least one of R_9, R_{10}, R_{11}, R_{12}, and R_{13} is not hydrido.

[0011] In a preferred embodiment

n is an integer selected from 1 through 3;

Y is $-(CH_2)_q-$ wherein q is 1 or 2;

R_1 is haloalkyl;

R_2 is hydrido;

R_3 is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, and haloalkyl;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, heteroaralkoxy, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, halocycloalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxy, halocycloalkoxy, halocycloalkoxyalkyl, hydroxy, amino, nitro, C1-C6 alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylsulfonyl, alkanoyl, aroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, cycloalkyl, cycloalkylalkanoyl, C3-C7 cycloalkylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, haloalkoxyalkyl, aryl, aryloxy, aralkoxy, aryloxyalkyl, heteroaryloxy, heteroaryloxyalkyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, carboalkoxyalkyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cyano, cycloalkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl and haloalkylthio,

with the proviso that at least one of R_4, R_5, R_6, R_7, and R_8 is not hydrido and with the further proviso that at least one of R_9, R_{10}, R_{11}, R_{12}, and R_{13} is not hydrido.

[0012] In a further preferred embodiment,

n is an integer selected from 1 through 3;

Y is $-(CH_2)_q-$ wherein q is 1 or 2;

R_1 is haloalkyl;

R_2 is hydrido;

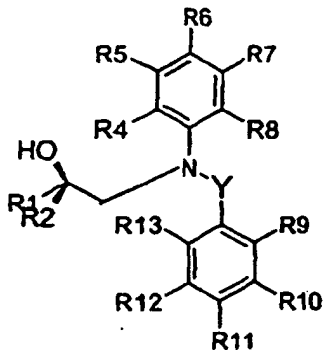
R_3 is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride, halo, and haloalkyl;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydride, heteroaralkoxy, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, perhaloaralkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxy, halocycloalkoxy, halocycloalkoxyalkyl, alkylthio, alkylthioalkyl, arylthio, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylsulfonyl, alkanoyl, haloalkanoyl, alkyl, cycloalkyl, C3-C7 cycloalkylalkyl, halo, haloalkyl, haloalkoxy, haloalkoxyalkyl, aryl, aryloxy, aralkoxy, aryloxyalkyl, heteroaryloxy, heteroaryloxyalkyl, carboalkoxy, carboalkoxyalkyl, carboaralkoxy and carbohaloalkoxy;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cycloalkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl and haloalkylthio.

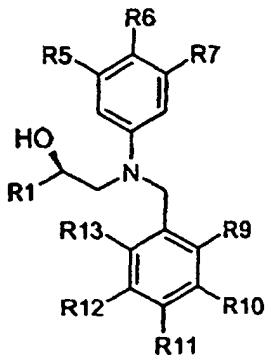
[0013] In a another preferred embodiment, the compounds of the invention are compounds of the following Formula D:



Formula "D"

wherein Y is $-CH_2-$;
wherein R^1 is haloalkyl;
wherein R^2 is hydrido;
wherein R^4 and R^8 are hydrido;
wherein R^5 and R^6 are selected from hydrido and alkoxy;
wherein R^7 is selected from aryloxy, arylalkoxy, 5,6,7,8-tetrahydronaphth-2-yloxy, alkoxy, cycloalkoxy, cycloalkylalkoxy and halo;
wherein said aryloxy and arylalkoxy groups in R^7 may be substituted at one or more substitutable positions with one or more radicals selected from halo, alkyl, alkoxy, haloalkoxy and haloalkyl;
wherein R^9 is selected from hydrido, halo and haloalkyl;
wherein R^{10} is selected from haloalkoxy, haloalkyl and haloalkylthio;
wherein R^{11} is selected from hydrido, halo and haloalkyl;
wherein R^{12} is selected from hydrido and haloalkyl;
wherein R^{13} is selected from hydrido, halo and haloalkyl.

[0014] In yet another preferred embodiment, the compounds of the invention are compounds of the following Formula C:



Formula "C"

wherein R^1 is selected from trifluoromethyl and chloromethyl;
wherein R^5 and R^6 are selected from hydrido and methoxy;
wherein R^7 is selected from phenyloxy, benzyloxy, 5,6,7,8-tetrahydronaphth-2-yloxy, isopropoxy, cyclopentoxy, bromo, cyclohexylmethoxy and methoxy;
wherein said phenyloxy and benzyloxy groups in R^7 may be substituted at one or more substitutable positions with one or more radicals selected from chloro, ethyl, trifluoromethoxy, bromo, fluoro, methyl, isopropyl, trifluoromethyl,

isopropoxy and tert-butyl;

wherein R^9 is selected from hydrido, fluoro and trifluoromethyl;

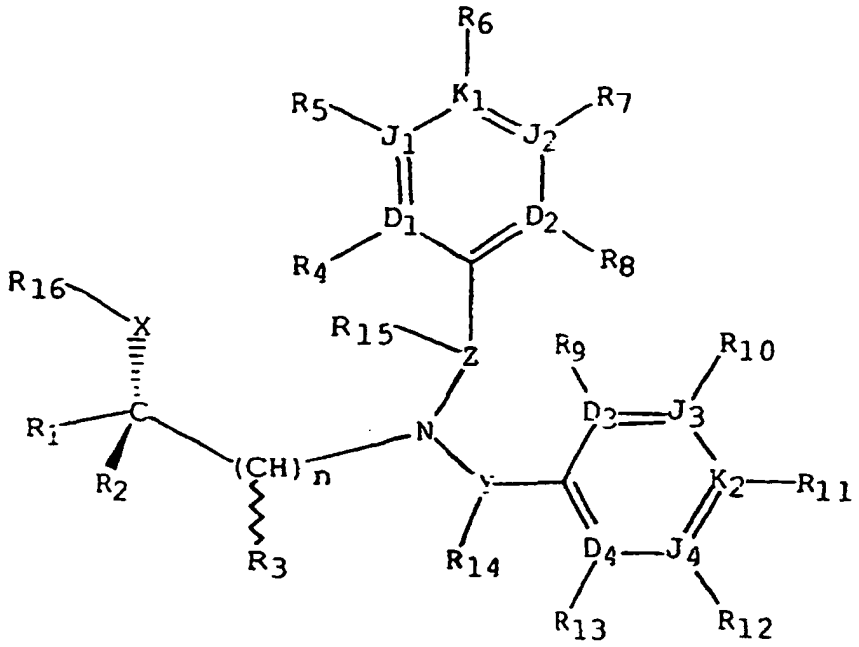
wherein R^{10} is selected from 1,1,2,2-tetrafluoroethoxy, trifluoromethoxy, pentafluoroethyl, trifluoromethyl and trifluoromethylthio;

wherein R^{11} is selected from hydrido, trifluoromethyl and fluoro;

wherein R^{12} is selected from hydrido and trifluoromethyl;

wherein R^{13} is selected from hydrido, fluoro and trifluoromethyl.

[0015] The compounds of Formula M are a sub-group of the compounds of the following Formula I-H (also referred to herein as generic polycyclic aryl and heteroaryl (R)-chiral halogenated 1-substitutedamino-(n + 1)-alkanols), which is described here (together with certain other sub-groups thereof, in particular, the compounds of Formulae I-C and I-CP) for purposes of reference, in particular, in connection with the discussion of synthetic procedures below. The references to compounds of Formula I-H are not intended to imply that the scope of the invention extends beyond that of the claims.



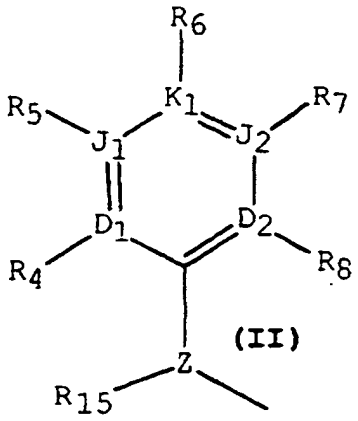
(I-H)

or a pharmaceutically-acceptable salt thereof, wherein;

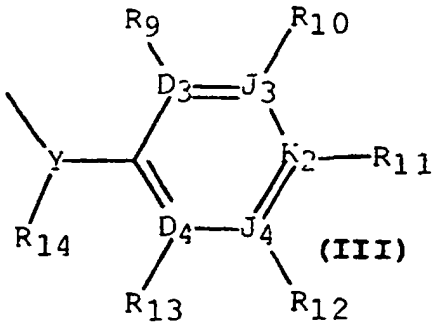
n is an integer selected from 1 through 4:

X is oxy;

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxymethyl, and haloalkenyloxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(A)Q wherein A is Formula (II) and Q is Formula (III);



(II)



(III)

R_{16} is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, alkoxyalkyl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, aralkoxyalkyl, heteroaralkoxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, monocarboalkoxyalkyl, monocarboalkoxy, dicarboalkoxyalkyl, monocarboxamido, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, acyl, aroyl, heteroaroyl, heteroaryloxyalkyl, dialkoxyphosphonoalkyl, trialkylsilyl, and a spacer selected from the group consisting of a covalent single bond and a linear spacer moiety having a chain length of 1 to 4 atoms linked to the point of bonding of any aromatic substituent selected from the group consisting of R_4, R_8, R_9, R_{13}, R_{14}, and R_{15} to form a heterocyclyl ring having from 5 through 10 contiguous members;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and covalent bond with the provisos that no more than one of D_1, D_2, J_1, J_2 and K_1 can be a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 can be O, no more than one of D_1, D_2, J_1, J_2 and K_1 can be S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 can be N;

D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, N, O, S and covalent bond with the provisos that no more than one can be a covalent bond, no more than one of D_3, D_4, J_3, J_4 and K_2 can be O, no more than one of D_3, D_4, J_3, J_4 and K_2 can be S, no more than two of D_3, D_4, J_3, J_4 and K_2 can be O and S, one of D_3, D_4, J_3, J_4 and K_2 must be a covalent bond when two of D_3, D_4, J_3, J_4 and K_2 are O and S, and no more than four of D_3, D_4, J_3, J_4 and K_2 can be N;

R_2 is hydrido;

R_2 can be selected from the group consisting of hydroxyalkyl, alkyl, alkenyl, alkynyl, aryl, aralkyl, aralkoxyalkyl, aryloxyalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, heteroaryl, heteroarylalkyl, heteroarylthioalkyl, perhaloaryl, perhaloaralkyl, perhaloaralkyl, heteroaralkylthioalkyl, monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, carboaralkoxy, dicyanoalkyl, carboalkoxycyanoalkyl, dialkoxyphosphonoalkyl, and diaralkoxyphosphonoalkyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(A)Q;

R_3 is selected from the group consisting of hydride, hydroxy, halo, cyano, aryloxy, hydroxyalkyl, amino, alkylamino, dialkylamino, acyl, acylamido, alkoxy, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, alkoxyalkyl, aralkoxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, aroyl, heteroaroyl, aralkylthioalkyl, heteroaralkylthioalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, heteroaryl, heteroarylalkyl, heteroarylthioalkyl, monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, arylsulfinylalkyl, arylsulfonylalkyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, carboaralkoxy, dialkoxyphosphonoalkyl, and diaralkoxyphosphonoalkyl with the provisos that $(CHR_3)_n$-N(A)Q has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from a group consisting of a covalent single bond, $(C(R_{14})_2)_q$ wherein q is an integer selected from

1 through 2 and $(CH(R_{14}))_g$-W-$(CH(R_{14}))_p$ wherein g and p are integers independently selected from 0 through 1;

R_{14} is independently selected from the group consisting of hydrido, hydroxy, halo, cyano, aryloxy, amino, alkylamino, dialkylamino, hydroxyalkyl, acyl, aroyl, heteroaroyl, heteroaryloxyalkyl, sulfhydryl, acylamido, alkoxy, alkylthio, arylthio, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, aralkoxyalkylalkoxy, alkylsulfinylalkyl, alkylsutfonylalkyl, aralkylthioalkyl, heteroaralkoxythioalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, heteroarylthioalkyl, heteroaralkylthioalkyl, monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, alkylsulfinyl, alkylsulfonyl, haloalkylsulfinyl, haloalkylsulfonyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, aralkylsulfinyl, aralkylsulfonyl, cycloalkylsulfinyl, cycloalkylsulfonyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinyl, heteroarylsulfonyl, heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, carboaralkoxy, dialkoxyphosphono, diaralkoxyphosphono, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, a spacer selected from a moiety having a chain length of 3 to 6 atoms connected to the point of bonding selected from the group consisting of R_9 and R_{13} to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 contiguous members and a heterocyclyl ring having from 5 through 8 contiguous members, and a spacer selected from a moiety having a chain length of 2 to 5 atoms connected to the point of bonding selected from the group consisting of R_4 and R_8 to form a heterocyclyl having from 5 through 8 contiguous members with the proviso that, when Y is a covalent bond, an R_{14} substituent is not attached to Y;

R_{14} and R_{15} can be taken together to form a spacer selected from a moiety having a chain length of 2 to 5 atoms to form a heterocyclyl ring having from 5 through 8 contiguous members;

R_{14} and R_{14}, when bonded to the different atoms, can be taken together to form a group selected from the group consisting of a covalent bond, alkylene, haloalkylene, and a spacer selected from a group consisting of a moiety having a chain length of 2 to 5 atoms connected to form a ring selected from the group of a saturated cycloalkyl having from 5 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, and a heterocyclyl having from 5 through 8 contiguous members;

R_{14} and R_{14}, when bonded to the same atom can be taken together to form a group selected from the group consisting of oxo, thiono, alkylene, haloalkylene, and a spacer selected from the group consisting of a moiety having a chain length of 3 to 7 atoms connected to form a ring selected from the group consisting of a cycloalkyl having from 4 through 8 contiguous members, a cycloalkenyl having from 4 through 8 contiguous members, and a heterocyclyl having from 4 through 8 contiguous members:

W is selected from the group consisting of O, C(O), C(S), C(O)N(R_{14}), C(S)N(R_{14}), (R_{14})NC(O), (R_{14})NC(S), S. S(O), $S(O)_2$, $S(O)_2N(R_{14})$, (R_{14})N$S(O)_2$, and N(R_{14}) with the proviso that R_{14} is selected from other than halo and cyano;

Z is independently selected from a group consisting of a covalent single bond, $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2, $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1 with the proviso that, when Z is a covalent single bond, an R_{15} substituent is not attached to Z;

R_{15} is independently selected, when Z is $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2, from the group consisting of hydrido, hydroxy, halo, cyano, aryloxy, amino, alkylamino, dialkylamino, hydroxyalkyl, acyl, aroyl, heteroaroyl, heteroaryloxyalkyl, sulfhydryl, acylamido, alkoxy, alkylthio, arylthio, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, aralkoxyalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, aralkylthioalkyl, heteroaralkylthioalkyl, alkoxyalkyl, heteroaryloxyalkyl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, heteroarylthioalkyl, heteroaralkylthioalkyl, monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, alkylsulfinyl, alkylsulfonyl, haloalkylsulfinyl, haloalkylsulfonyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, aralkylsulfinyl, aralkylsulfonyl, cycloalkylsulfinyl, cycloalkylsulfonyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinyl, heteroarylsulfonyl, heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxy, carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, carboaralkoxy, dialkoxyphosphono, diaralkoxyphosphono, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, a spacer selected from a moiety having a chain length of 3 to 6 atoms connected to the point of bonding selected from the group consisting of R_4 and R_8 to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 contiguous members and a heterocyclyl ring having from 5 through 8 contiguous members, and a spacer selected from a moiety having a chain length of 2 to 5 atoms connected to the point of bonding selected from the group consisting of R_9 and R_{13} to form a heterocyclyl having from 5 through 8 contiguous members;

R_{15} and R_{15}, when bonded to the different atoms, can be taken together to form a group selected from the group consisting of a covalent bond, alkylene, haloalkylene, and a spacer selected from a group consisting of a moiety having a chain length of 2 to 5 atoms connected to form a ring selected from the group of a saturated cycloalkyl having from

5 through 8 contiguous members, a cycloalkenyl having from 5 through 8 contiguous members, and a heterocyclyl having from 5 through 8 contiguous members;

R_{15} and R_{15}, when bonded to the same atom, can be taken together to form a group selected from the group consisting of oxo, thiono, alkylene, haloalkylene, and a spacer selected from the group consisting of a moiety having a chain length of 3 to 7 atoms connected to form a ring selected from the group consisting of a cycloalkyl having from 4 through 8 contiguous members, a cycloalkenyl having from 4 through 8 contiguous members, and a heterocyclyl having from 4 through 8 contiguous members;

R_{15} is independently selected, when Z is $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1, from the group consisting of hydrido, halo, cyano, aryloxy, carboxyl, acyl, aroyl, heteroaroyl, hydroxyalkyl, heteroaryloxyalkyl, acylamido, alkoxy, alkylthio, arylthio, alkyl, alkenyl, alkynyl, aryl, aralkyl, aryloxyalkyl, alkoxyalkyl, heteroaryloxyalkyl, aralkoxyalkyl, heteroaralkoxyalkyl, alkylsulfonylalkyl, alkylsulfinylalkyl, alkenyloxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkenyl, cycloalkenylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroaralkyl, heteroarylthioalkyl, heteroaralkylthioalkyl, monocarboalkoxyalkyl, dicarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, alkylsulfinyl, alkylsulfonyl, haloalkylsulfinyl, haloalkylsulfonyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, aralkylsulfinyl, aralkylsulfonyl, cycloalkylsulfinyl, cycloalkylsulfonyl, cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl, heteroarylsulfinyl, heteroarylsulfonyl, heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, carboxyalkyl, carboalkoxy, carboxamide, carboxamidoalkyl, carboaralkoxy, dialkoxyphosphonoalkyl, diaralkoxyphosphonoalkyl, a spacer selected from a linear moiety having a chain length of 3 to 6 atoms connected to the point of bonding selected from the group consisting of R_4 and R_8 to form a ring selected from the group consisting of a cycloalkenyl ring having from 5 through 8 contiguous members and a heterocyclyl ring having from 5 through 8 contiguous members, and a spacer selected from a linear moiety having a chain length of 2 to 5 atoms connected to the point of bonding selected from the group consisting of R_9 and R_{13} to form a heterocyclyl ring having from 5 through 8 contiguous members;

R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and R_{13} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroaralkyl, heteroarylaminoalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl with the proviso that there are one to five non-hydrido ring substituents R_4, R_5, R_6, R_7, and R_8 present, that there are one to five non-hydride ring substituents R_9, R_{10}, R_{11}, R_{12}, and R_{13} present, and R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and R_{13} are each independently selected to maintain the tetravalent nature of carbon, trivalent nature of nitrogen, the divalent nature of sulfur, and the divalent nature of oxygen;

R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, can be used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be used at the same time;

R_4 and R_9, R_4 and R_{13}, R_8 and R_9, and R_8 and R_{13} can be independently selected to form a spacer pair wherein

said spacer pair is taken together to form a linear moiety wherein said linear moiety forms a ring selected from the group consisting of a partially saturated heterocyclyl ring having from 5 through 8 contiguous members and a heteroaryl ring having from 5 through 6 contiguous members with the proviso that no more than one of the group consisting of spacer pairs R_4 and R_9, R_4 and R_{13}, R_8 and R_9, and R_8 and R_{13} can be used at the same time;

R_5 and R_{10}, R_5 and R_{12}, R_7 and R_{10}, and R_7 and R_{12} can be independently selected to form a spacer pair wherein said spacer pair is taken together to form a linear moiety wherein said linear moiety forms a C8 to C13 heterocyclyl ring having from 8 through 13 contiguous members with the proviso that no more than one of the group consisting of spacer pairs R_5 and R_{10}, R_5 and R_{12}, R_7 and R_{10}, and R_7 and R_{12} can be used at the same time, and K_2 can be S, one of D_3, D_4, J_3, J_4 and K_2 must be a covalent bond when two of D_3, D_4, J_3, J_4 and K_2 are O and S, and no more than four of D_3, D_4, J_3, J_4 and K_2 can be N;

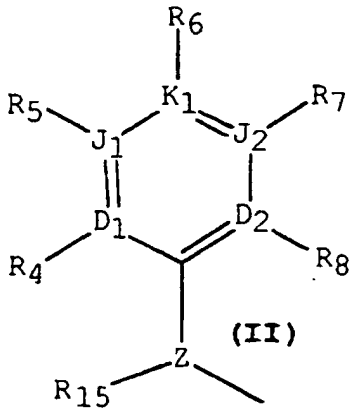
D_1, D_2, J_1, J_2 and K_1 can be selected from the group consisting of C, O, S, N and covalent bond with the provisos that D_3, D_4, J_3, J_4 and K_2 are each carbon and at least one of D_1, D_2, J_1, J_2 and K_1 is selected from the group consisting of O, S, and N wherein, when D_1, D_2, J_1, J_2 and K_1 are selected from the group consisting of C, O, S, covalent bond, and N, no more than one of D_1, D_2, J_1, J_2 and K_1 can be a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 can be O, no more than one of D_1, D_2, J_1, J_2 and K_1 can be S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 can be N;

n is an integer selected from 1 through 4;

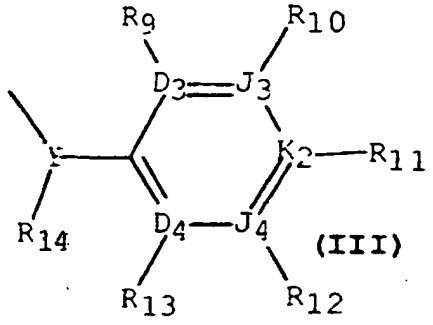
X is oxy;

R_{16} is selected from the group consisting of hydrido, acyl, aroyl, and trialkylsilyl;

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxymethyl, and haloalkenyloxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(A)Q wherein A is Formula (II) and Q is Formula (III);



(II)



(III)

R_2 is hydrido;

R_2 can be selected from the group consisting of aryl, aralkyl, alkyl, alkenyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, dicyanoalkyl, and carboalkoxycyanoalkyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(A)Q;

R_3 is selected from the group consisting of hydrido, hydroxy, cyano, aryl, aralkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, heteroaryl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl with the provisos that $(CHR_3)_n$-N(A)Q has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from the group consisting of covalent single bond and $(C(R_{14})_2)_q$ wherein q is an integer selected from 1 through 2;

R_{14} is selected from the group consisting of hydrido, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl;

Z is selected from the group consisting of covalent single bond, $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2. and $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1;

W is oxy;

R_{15} is selected from the group consisting of hydride, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl,

haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl ;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroarylsulfonyl, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, cycloalkoxy, cycloalkylalkoxy, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, arylamino, aralkylamino, arylthio, arylthioalkyl, alkylsulfonyl, alkylsulfonamido, monoarylamidosulfonyl, arylsulfonyl, heteroarylthio, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyalkyl, aryl, aryloxy, aralkoxy, saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, heteroaralkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboxamido, carboxamidoalkyl, and cyano;

R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} spacer pairs can be independently selected from the group consisting of alkylene, alkenylene, alkylenedioxy, aralkylene, diacyl, haloalkylene, and aryloxylene with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 can be used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be used at the same time.

[0016] In an even more specific embodiment of compounds Formula I-H,

D_1, D_2, J_1, J_2 and K_1 are each carbon;

D_3, D_4, J_3, J_4 and K_2 are independently selected from the group consisting of C, N, O, S and covalent bond with the provisos that at least one of D_3, D_4, J_3, J_4 and K_2 is selected from the group consisting of O, S, and N, wherein no more than one of D_3, D_4, J_3, J_4 and K_2 can be a covalent bond, no more than one of D_3, D_4, J_3, J_4 and K_2 can be O, no more than one of D_3, D_4, J_3, J_4 and K_2 can be S, one of D_3, D_4, J_3, J_4 and K_2 must be a covalent bond when two of D_3, D_4, J_3, J_4 and K_2 are O and S, and no more than four of D_3, D_4, J_3, J_4 and K_2 can be N;

n is an integer selected from 1 to 3;

X is oxy;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, chloromethyl, fluoromethyl, difluoromethyl, chlorodifluoromethyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, and heptafluoropropyl;

R_{16} is selected from the group consisting of acetyl, benzoyl, dimethyl *tert* -butylsilyl, hydrido, and trimethylsilyl;

R_2 is hydrido;

R_2 can be selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, isopropyl, isobutyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, chloromethyl, trifluoromethoxymethyl, fluoromethyl, difluoromethyl, 2,2,3,3,3-pentafluoropropyl, and pentafluorophenoxymethyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(A)Q:

R_3 is selected from the group consisting of hydride, hydroxy, cyano, acetyl, methoxy, ethoxy, methyl, ethyl, propyl, vinyl, phenyl, methoxymethyl, 4-trifluoromethylphenyl, trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, chloromethyl, fluoromethyl, difluoromethyl, chlorodifluoromethyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, heptafluoropropyl, pentafluorophenyl, and pentafluorophenoxymethyl with the provisos that $(CHR_3)_n$-N(A)Q has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2.

[0017] In another even more specific embodiment of compounds Formula I-H,

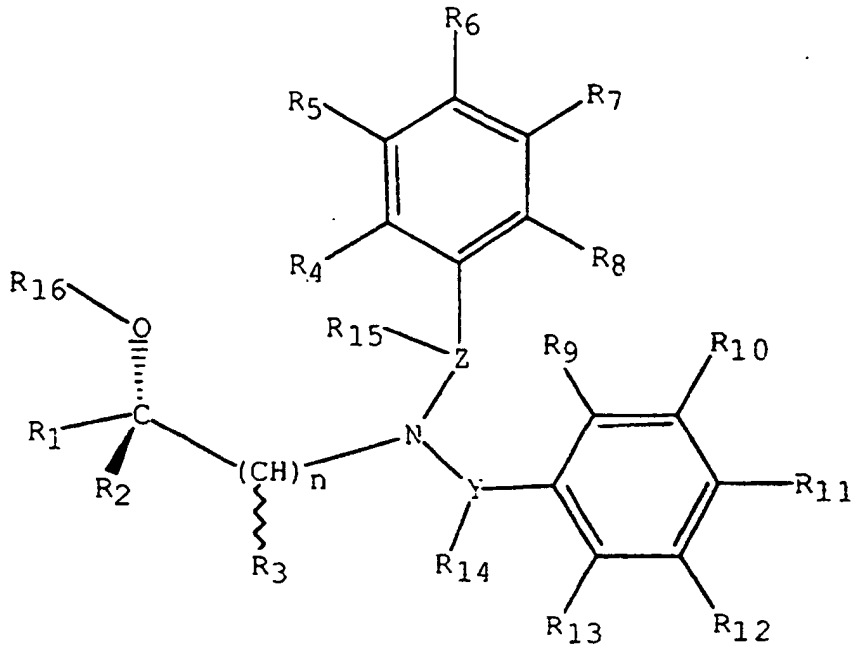
D_3, D_4, J_3, J_4 and K_2 are each carbon;

D_1, D_2, J_1, J_2 and K_1 are independently selected from the group consisting of C, N, O, S and covalent bond with the provisos that at least one of D_1, D_2, J_1, J_2 and K_1 is selected from the group consisting of O, S, and N, wherein no more than one of D_1, D_2, J_1, J_2 and K_1 can be a covalent bond, no more than one of D_1, D_2, J_1, J_2 and K_1 can be O, no more than one of D_1, D_2, J_1, J_2 and K_1 can be S, one of D_1, D_2, J_1, J_2 and K_1 must be a covalent bond when two of D_1, D_2, J_1, J_2 and K_1 are O and S, and no more than four of D_1, D_2, J_1, J_2 and K_1 can be N;

n is an integer selected from 1 to 3;

X is oxy;

[0018] In a specific sub-group of compounds of Formula I-H, the compounds correspond to the Formula I-C (also referred to herein as phenyl (R)-chiral halogenated 1-substitutedamino-(n+1)-alkanols):



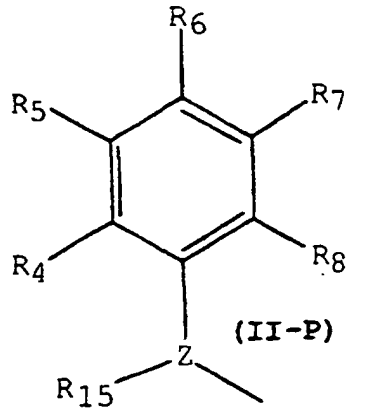
(I-C)

or a pharmacuetically acceptable salt thereof, wherein:

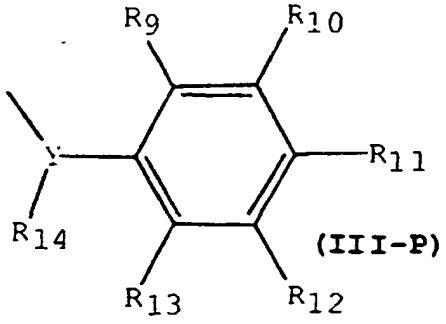
n is an integer selected from 1 through 4;

R_{16} is selected from the group consisting of hydrido, alkyl, acyl, aroyl, heteroaroyl, trialkylsilyl, and a spacer selected from the group consisting of a covalent single bond and a linear spacer moiety having a chain length of 1 to 4 atoms linked to the point of bonding of any aromatic substituent selected from the group consisting of R_4, R_8, R_9, and R_{13} to form a heterocyclyl ring having from 5 through 10 contiguous members with the proviso that said linear spacer moiety is other than covalent single bond when R_2 is alkyl;

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxymethyl, and haloalkenyloxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)



(III-P)

R_2 is hydrido:

R_2 can be selected from the group consisting of aryl, aralkyl, alkyl, alkenyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, dicyanoalkyl, and carboalkoxycyanoalkyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp:

R_3 is selected from the group consisting of hydrido, hydroxy, cyano, aryl, aralkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, heteroaryl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, mono-

cyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from the group consisting of covalent single bond and $(C(R_{14})_2)_q$ wherein q is an integer selected from 1 through 2;

R_{14} is selected from the group consisting of hydrido, hydroxy, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, carboxamidoalkyl;

Z is selected from the group consisting of covalent single bond, $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1;

W is selected from the group consisting of O, C(O), C(S), $C(O)N(R_{14})$, $C(S)N(R_{14})$, $(R_{14})NC(O)$, $(R_{14})NC(S)$, S, S(O), $S(O)_2$, $S(O)_2N(R_{14})$, $(R_{14})NS(O)_2$, and $N(R_{14})$ with the proviso that R_{14} is other than cyano:

R_{15} is selected from the group consisting of hydrido, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, and carboxamidoalkyl;

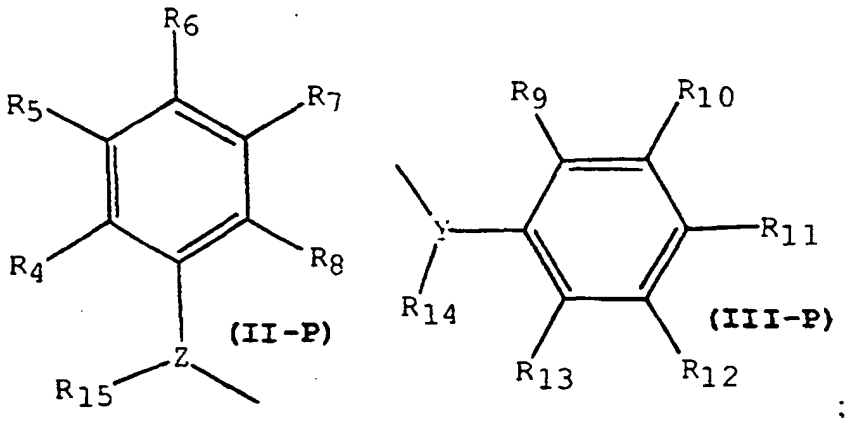
R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cyctoalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, heteroaralkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8, can be used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be used at the same time.

R_{16} is selected from the group consisting of hydride, acyl, aroyl, and trialkylsilyl;

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxymethyl, and haloalkenyloxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



R_2 is hydrido;

R_2 can be selected from the group consisting of aryl, aralkyl, alkyl, alkenyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, dicyanoalkyl, and carboalkoxycyanoalkyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

R_3 is selected from the group consisting of hydrido, hydroxy, cyano, aryl, aralkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, heteroaryl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from the group consisting of covalent single bond and $(C(R_{14})_2)_q$ wherein q is an integer selected from 1 through 2;

R_{14} is selected from the group consisting of hydrido, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl;

Z is selected from the group consisting of covalent single bond, $(C(R_{15})_2)_q$ wherein q is an integer selected from 1 through 2, and $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1;

W is oxy;

R_{15} is selected from the group consisting of hydride, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboxamide, and carboxamidoalkyl;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl ;

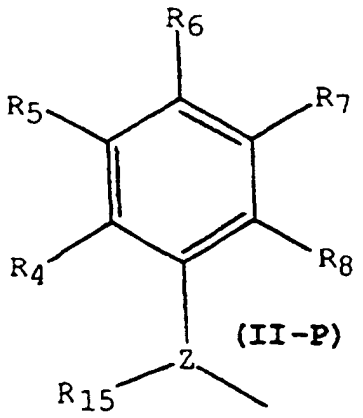
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroarylsulfonyl, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, cycloalkoxy, cycloalkylalkoxy, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, arylamino, aralkylamino, arylthio, arylthioalkyl, alkylsulfonyl, alkylsulfonamido, monoarylamidosulfonyl, arylsulfonyl, heteroarylthio, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboxamido, carboxamidoalkyl, and cyano;

R_4 and R_5, R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} spacer pairs can be independently selected from the group consisting of alkylene, alkenylene, alkylenedioxy, aralkylene, diacyl, haloalkylene, and aryloxylene with the provisos that no more than one of the group consisting of spacer pairs R_4 and R_5, R_5 and R_6, R_6 and R_7, and R_7 and R_8 can be used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be used at the same time.

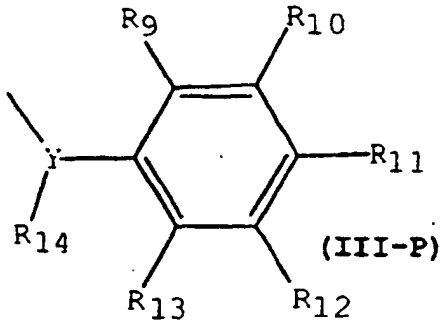
[0019] In a more preferred embodiment of compounds of Formula 1-C,

n is an integer selected from 1 through 2;

R_1 is selected from the group consisting of haloalkyl and haloalkoxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)



(III-P)

R_{16} is hydrido;

R_2 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, haloalkoxy, haloalkoxyalkyl, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, and heteroaryl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

R_3 is selected from the group consisting of hydrido, aryl, alkyl, alkenyl, haloalkyl, and haloalkoxyalkyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from the group consisting of a covalent single bond and alkylene;

Z is selected from the group consisting of a covalent single bond and alkylene;

R_{14} is selected from the group consisting of hydrido, alkyl, and haloalkyl;

R_{15} is selected from the group consisting of hydrido, alkyl, and haloalkyl;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride and halo;

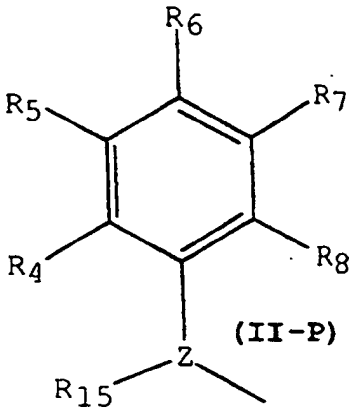
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, heterocyclyloxy, aralkylaryl, heteroaryloxyalkyl, heteroarylthio, and heteroarylsulfonyl.

[0020] In an even more preferred embodiment of compounds of Formula I-C,

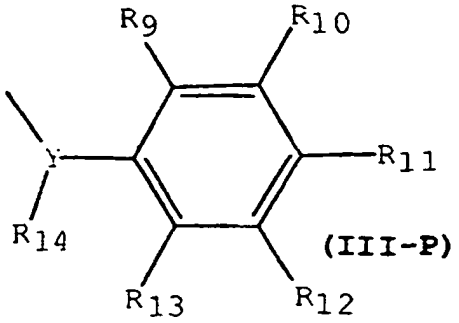
n is the integer 1;

R_{16} is hydrido;

R_1 is haloalkyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)



(III-P)

R_2 is hydride;

R_2 can be selected from the group consisting of alkyl, haloalkyl, aryl, and haloalkoxy with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

R_3 is selected from the group consisting of hydrido, alkyl, and haloalkyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is alkylene;

Z is covalent single bond;

R_{14} is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride and halo;

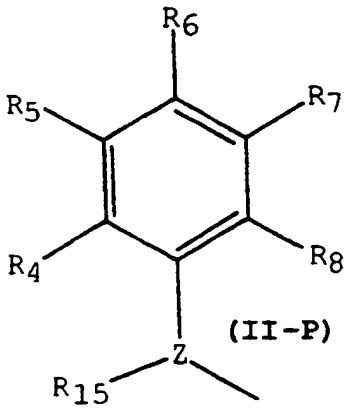
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, alkyl, halo, haloalkyl, haloalkoxy, aryl, alkylthio, arylamino, arylthio, aroyl, arylsulfonyl, aryloxy, aralkoxy, heteroaryloxy, alkoxy, aralkyl, cycloalkoxy, cycloalkylalkoxy, cycloalkylalkanoyl, heteroaryl, cycloalkyl, haloalkylthio, hydroxyhaloalkyl, heteroaralkoxy, and heteroaryloxyalkyl.

[0021] In an embodiment of compounds of Formula I-C,

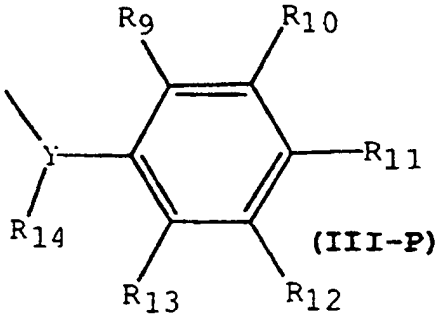
n is an integer selected from 1 to 3;

R_1 is selected from the group consisting of trifluoromethyl,

1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, chloromethyl, fluoromethyl, difluoromethyl, chlorodifluoromethyl, pentafluoroethyl, 2,2,3,3,3-pentafluoropropyl, and heptafluoropropyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)



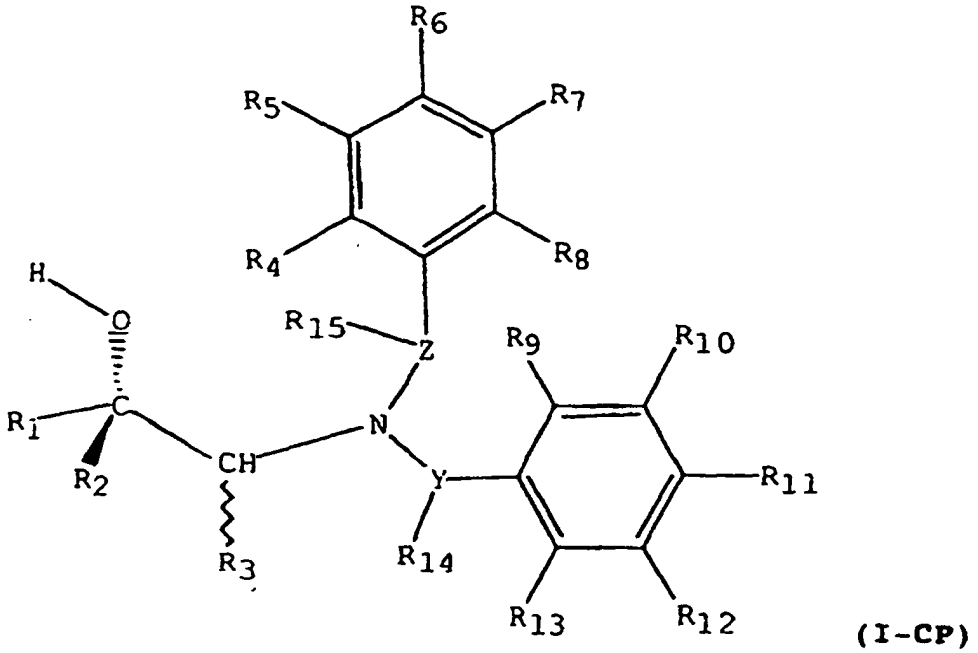
(III-P)

R_{16} is selected from the group consisting of acetyl, benzoyl, dimethyl *tert* -butylsilyl, hydrido, and trimethylsilyl;

R_2 is hydrido;

R_2 can be selected from the group consisting of methyl, ethyl, propyl, butyl, isopropyl, isobutyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, chloromethyl, trifluoromethoxymethyl, fluoromethyl, difluoromethyl, 2,2,3,3,3-pentafluoropropyl, and and pentafluorophenoxymethyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

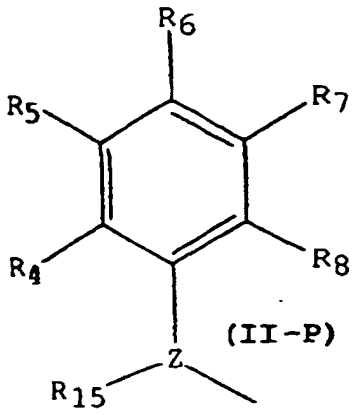
[0022] In a specific sub-group of compounds of Formula I-C, compounds have the Formula I-CP:



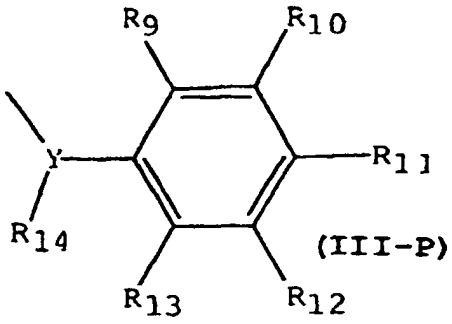
(I-CP)

or a pharmaceutically acceptable salt thereof, wherein;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)



(III-P)

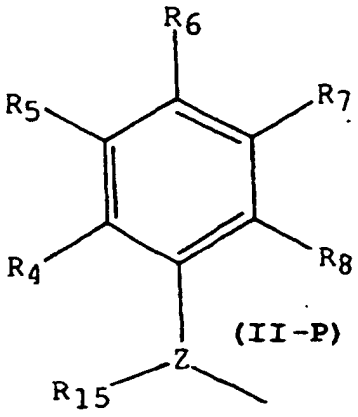
R_2 is hydrido;

R_2 can be selected from the group consisting of methyl, ethyl, propyl, butyl, vinyl, phenyl, 4-trifluoromethylphenyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, and 2,2,3,3,3-pentafluoropropyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

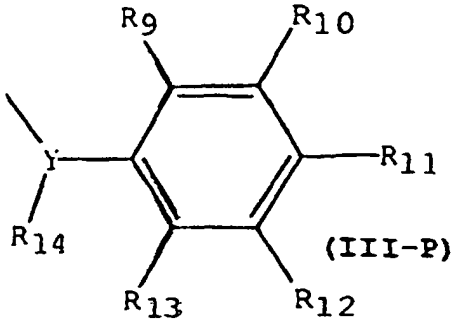
R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, ethyl, vinyl, methoxymethyl, trifluoromethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2.

[0023] In a specific sub-group of compounds of Formula I-CP,

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P):



(II-P)



(III-P)

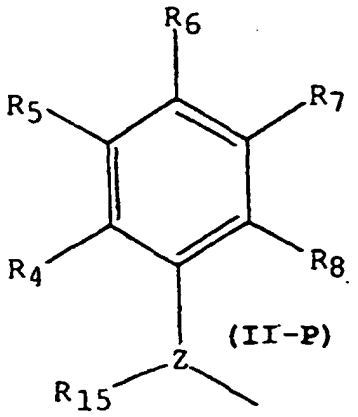
R_2 is hydrido:

R_2 can be selected from the group consisting of methyl, ethyl, phenyl, 4-trifluoromethylphenyl, trifluoromethoxymethyl, 1,1,2,2-tetrafluoroethoxymethyl, difluoromethyl, and 2,2,3,3,3-pentafluoropropyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

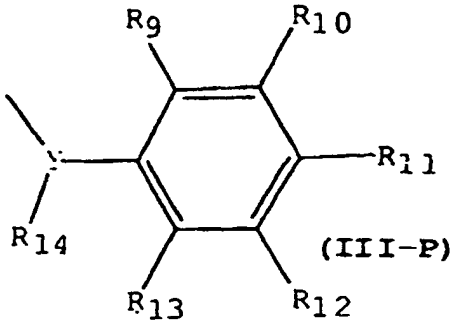
R_3 is selected from the group consisting of hydrido, phenyl, 4-trifluoromethylphenyl, methyl, trifluoromethyl, difluoromethyl, and chlorodifluoromethyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2.

[0024] In a further specific sub-group of compounds of Formula I-CP,

R_1 is selected from the group consisting of trifluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Ap)Qp wherein Ap is Formula (II-P) and Qp is Formula (III-P);



(II-P)

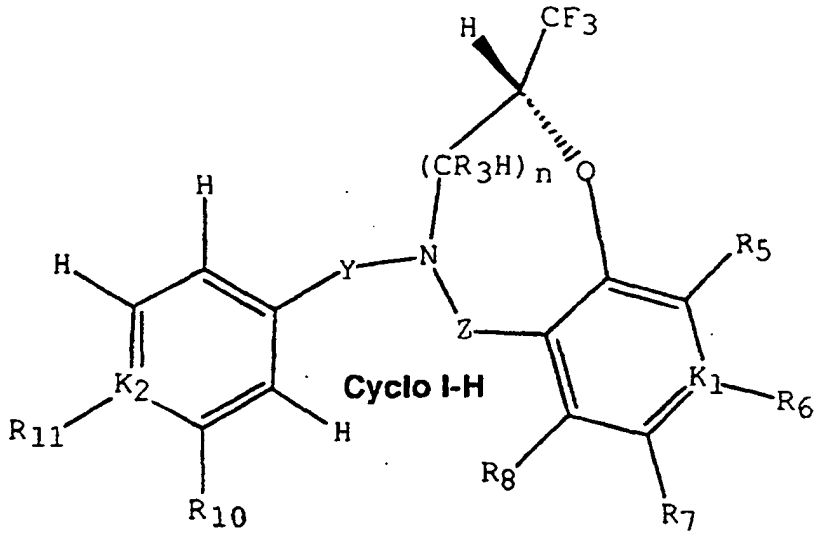


(III-P)

R_2 is hydrido;

R_2 can be phenyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Ap)Qp;

R_3 is selected from the group consisting of hydrido, methyl, trifluoromethyl, and difluoromethyl with the provisos that $(CHR_3)_n$-N(Ap)Qp has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2.

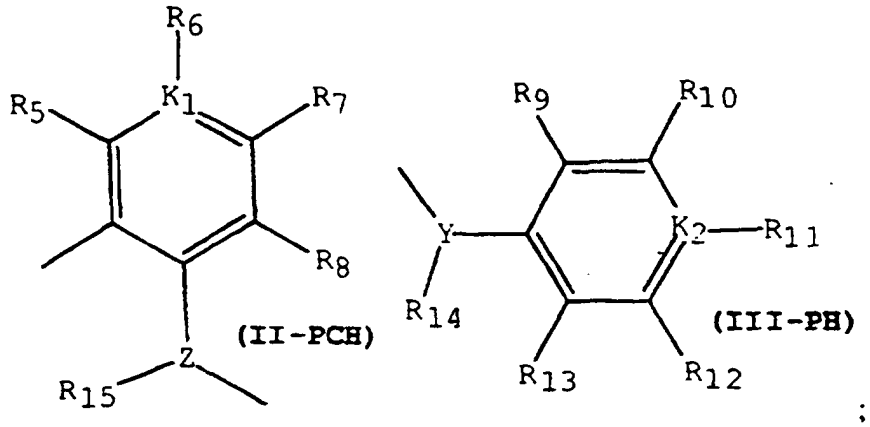


wherein:

K_1 and K_2 are independently selected from the group consisting of C and N;

n is an integer selected from 1 through 3:

R_1 is selected from the group consisting of haloalkyl, haloalkenyl, haloalkoxymethyl, and haloalkenyloxymethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Apch)Qph wherein Apch is Formula (II-PCH) and Qph is Formula (III-PH);



R_2 is hydrido;

R_2 is selected from the group consisting of aryl, aralkyl, alkyl, alkenyl, alkoxyalkyl, alkenyloxyalkyl, haloalkyl, haloalkenyl, halocycloalkyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, halocycloalkoxy, perhaloaryl, perhaloaralkyl, perhaloaryloxyalkyl, heteroaryl, heteroarylalkyl, dicyanoalkyl, and carboalkoxycyanoalkyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Apch)Qph;

R_3 is selected from the group consisting of hydride, hydroxy, halo, cyano, aryl. aralkyl, acyl, alkoxy, alkyl, alkenyl, alkoxyalkyl, heteroaryl, alkenyloxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboxamide, and carboxamidoalkyl with the provisos that $(CHR_3)_n$-N(Apch)Qph has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2;

Y is selected from the group consisting of a covalent single bond and $(C(R_{14})_2)_q$ wherein q is an integer selected from 1 through 2;

R_{14} is selected from the group consisting of hydride, hydroxy, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocarboalkoxyalkyl,

monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, and carboxamidoalkyl;

Z is selected from the group consisting of covalent single bond, $(C(R_{15})_2)_q$) wherein q is an integer selected from 1 through 2, and $(CH(R_{15}))_j$-W-$(CH(R_{15}))_k$ wherein j and k are integers independently selected from 0 through 1;

W is selected from the group consisting of O, C(O), S, S(O), and $S(O)_2$;

R_{15} is selected from the group consisting of hydrido, cyano, hydroxyalkyl, acyl, alkoxy, alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, haloalkenyl, haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, monocarboalkoxyalkyl, monocyanoalkyl, dicyanoalkyl, carboalkoxycyanoalkyl, carboalkoxy, carboxamide, and carboxamidoalkyl;

R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl;

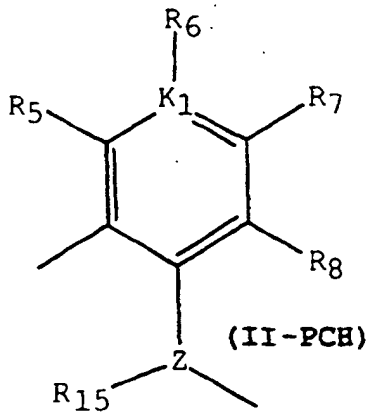
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl,haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, heteroaralkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

R_5 and R_6, R_6 and R_7, R_7 and R_8, R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be independently selected to form spacer pairs wherein a spacer pair is taken together to form a linear moiety having from 3 through 6 contiguous atoms connecting the points of bonding of said spacer pair members to form a ring selected from the group consisting of a cycloalkenyl ring having 5 through 8 contiguous members, a partially saturated heterocyclyl ring having 5 through 8 contiguous members, a heteroaryl ring having 5 through 6 contiguous members, and an aryl with the provisos that no more than one of the group consisting of spacer pairs R_5 and R_6, R_6 and R_7, and R_7 and R_8, can be used at the same time and that no more than one of the group consisting of spacer pairs R_9 and R_{10}, R_{10} and R_{11}, R_{11} and R_{12}, and R_{12} and R_{13} can be used at the same time.

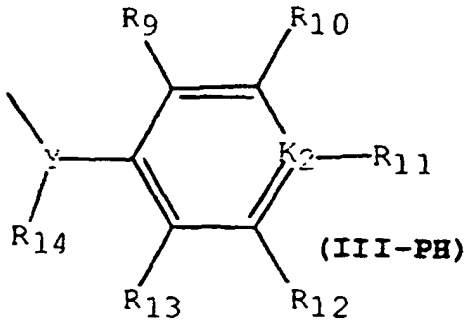
[0025] In an embodiment of compounds of Formula Cyclo I-H,

n is the integer 1;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the proviso that R_1 has a higher Cahn-Ingold-Prelog stereochemical system ranking than both R_2 and $(CHR_3)_n$-N(Apch)Qph wherein Apch is Formula (II-PCH) and Qph is Formula (III-PH);



(II-PCH)



(III-PH)

R_2 is hydrido;

R_2 is selected from the group consisting of phenyl, 4-trifluoromethylphenyl, vinyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, and 2,2,3,3,3-pentafluoropropyl with the proviso that R_2 has a lower Cahn-Ingold-Prelog system ranking than both R_1 and $(CHR_3)_n$-N(Apch)Qph;

R_3 is selected from the group consisting of hydrido, methyl, ethyl, vinyl, phenyl, 4-trifluoromethylphenyl, methoxymethyl, trifluoromethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl with the provisos that $(CHR_3)_n$-N(Apch)Qph has a lower Cahn-Ingold-Prelog stereochemical system ranking than R_1 and a higher Cahn-Ingold-Prelog stereochemical system ranking than R_2.

[0026] In another embodiment of compounds of Formula Cyclo I-H,

n is the integer 1;

R_1 is selected from the group consisting of trifluoromethyl, 1,1,2,2-tetrafluoroethoxymethyl, trifluoromethoxymethyl, difluoromethyl, chlorodifluoromethyl, and pentafluoroethyl;

R_2 is hydrido;

[0027] In a preferred embodiment of compounds of the invention,

Y is selected from the group consisting of methylene, ethylene, and ethylidene;

Z is covalent single bond;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride and fluoro with the proviso that there is no R_4, R_8, R_9, or R_{13} when the embodiment is a compound of Formula Cyclo I-H;

R_5 and R_{10} are independently selected from the group consisting of 4-aminophenoxy, benzoyl, benzyl, benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-bromo-2-nitrophenoxy, 3-bromobenzyloxy, 4-bromobenzytoxy, 4-bromophenoxy, 5-bromopyrid-2-yloxy, 4-butoxyphenoxy, chloro, 3-chlorobenzyl, 2-chlorophenoxy, 4-chlorophenoxy, 4-chloro-3-ethylphenoxy, 3-chloro-4-fluorobenzyl, 3-chloro-4-fluorophenyl, 3-chloro-2-fluorobenzyloxy, 3-chlorobenzyloxy, 4-chlorobenzyloxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, 2-cyanopyrid-3-yloxy, 4-cyanophenoxy, cyclobutoxy, cyclobutyl, cyclohexoxy, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropyl, cyclopropylmethoxy, cyclopropoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3,5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 2,4-difluorobenzyloxy, 3,4-difluorobenzyloxy, 2,5-difluorobenzyloxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 3,5-difluorobenzyloxy, 4-difluoromethoxybenzyloxy, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3,4-dimethylbenzyl, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 2,2-dimethylpropoxy, 1,3-dioxan-2-yl, 1,4-dioxan-2-yl, 1,3-dioxolan-2-yl, ethoxy, 4-ethoxyphenoxy, 4-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, fluoro, 4-fluoro-3-methylbenzyl, 4-fluoro-3-methylphenyl, 4-fluoro-3-methylbenzoyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 4-fluoro-2-trifluoromethylbenzyloxy, 4-fluoro-3-trifluoromethylbenzyloxy, 2-fluorophenoxy, 4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 4-fluoropyrid-2-yloxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, 3-iodobenzyloxy, isobutyl, isobutylamino, isobutoxy, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, isopropyl, 4-isopropylbenzyloxy, 3-isopropylphenoxy, 4-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxycarbonylbutoxy, 3-methoxycarbonylprop-2-enyloxy, 4-methoxyphenyl, 3-methoxyphenylamino, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenzyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 4-nitrophenylthio, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, phenylsulfonyl, 4-propanoylphenoxy, propoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl, *sec*-butyl, 4-*sec*-butylphenoxy,*tert* -butoxy, 3-*tert* -butylphenoxy, 4-*tert* -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,3,5-trifluorobenzyloxy, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 3-trifluoromethoxyphenoxy, 4-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 4-trifluoromethylbenzyloxy, 2,4-bis-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 3-trifluoromethylthiobenzyloxy, 4-trifluoromethylthiobenzyloxy, 2,3,4-trifluorophenoxy, 2,3,4-trifluorophenyl, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 3-trifluoromethylthiophenoxy, and trifluoromethylthio;

R_6 and R_{11} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, trifluoromethyl, and trifluoromethoxy;

R_7 and R_{12} are independently selected from the group consisting of hydrido, fluoro, and trifluoromethyl.

[0028] In an even more preferred embodiment of compounds of the invention,

Y is methylene;

Z is covalent single bond;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido and fluoro with the proviso that there is no R_4, R_8, R_9, or R_{13} when the embodiment is a compound of Formula Cyclo I-H;

R_5 and R_{10} are independently selected from the group consisting of benzyloxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 3-bromobenzyloxy, 4-bromophenoxy,4-butoxyphenoxy, 3-chlorobenzyloxy, 2-chlorophenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 2-chloro-4-fluorophenoxy, 4-chloro-2-fluorophenoxy, 4-chlorophenoxy, 3-chloro-4-ethylphenoxy, 3-chloro-4-methylphenoxy,3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 4-chlorophenylamino, 5-chloropyrid-3-yloxy, cyclobutoxy, cyclobutyl, cyclohexylmethoxy, cyclopentoxy, cyclopentyl, cyclopentylcarbonyl, cyclopropylmethoxy, 2,3-dichlorophenoxy, 2,4-dichlorophenoxy, 2,4-dichlorophenyl, 3.5-dichlorophenyl, 3,5-dichlorobenzyl, 3,4-dichlorophenoxy, 3,4-difluorophenoxy, 2,3-difluorobenzyloxy, 3,5-difluorobenzyloxy, difluoromethoxy, 3,5-difluorophenoxy, 3,4-difluorophenyl, 2,3-difluorophenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,5-dimethoxyphenoxy, 3-dimethylaminophenoxy, 3,4-dimethylbenzyloxy, 3,5-dimethylbenzyloxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 1,3-dioxolan-2-yl, 3-ethylbenzyloxy, 3-ethylphenoxy, 4-ethylaminophenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylbenzyl, 4-fluorobenzyloxy, 2-fluoro-3-methylphenoxy, 3-fluoro-4-methylphenoxy, 3-fluorophenoxy, 3-fluoro-2-nitrophenoxy, 2-fluoro-3-trifluoromethylbenzyloxy, 3-fluoro-5-trifluoromethylbenzyloxy, 2-fluorophenoxy,4-fluorophenoxy, 2-fluoro-3-trifluoromethylphenoxy, 2-fluorobenzyloxy, 4-fluorophenylamino, 2-fluoro-4-trifluoromethylphenoxy, 2-furyl, 3-furyl, heptafluoropropyl, 1,1,1,3,3,3-hexafluoropropyl, 2-hydroxy-3,3,3-trifluoropropoxy, isobutoxy, isobutyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, isopropoxy, 3-isopropylbenzyloxy, 3-isopropylphenoxy, isopropylthio, 4-isopropyl-3-methylphenoxy, 3-isothiazolyl, 4-isothiazolyl, 5-isothiazolyl, 3-methoxybenzyl, 4-methoxyphenylamino, 3-methylbenzyloxy, 4-methylbenxyloxy, 3-methylphenoxy, 3-methyl-4-methylthiophenoxy, 4-methylphenoxy, 1-methylpropoxy, 2-methylpyrid-5-yloxy, 4-methylthiophenoxy, 2-naphthyloxy, 2-nitrophenoxy, 4-nitrophenoxy, 3-nitrophenyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, pentafluoroethyl, pentafluoroethylthio, 2,2,3,3,3-pentafluoropropyl, 1,1,3,3,3-pentafluoropropyl, 1,1,2,2,3-pentafluoropropyl, phenoxy, phenylamino, 1-phenylethoxy, 4-propylphenoxy, 4-propoxyphenoxy, thiophen-3-yl.tert -butoxy, 3-tert -butylphenoxy, 4-tert -butylphenoxy, 1,1,2,2-tetrafluoroethoxy, tetrahydrofuran-2-yl, 2-(5,6,7,8-tetrahydronaphthyloxy), thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, thiophen-2-yl, 2,2,2-trifluoroethoxy, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-2-hydroxypropyl, trifluoromethoxy, 3-trifluoromethoxybenzyloxy, 4-trifluoromethoxybenzyloxy, 4-trifluoromethoxyphenoxy, 3-trifluoromethoxyphenoxy, trifluoromethyl, 3-trifluoromethylbenzyloxy, 1,1-bis-trifluoromethyl-1-hydroxymethyl, 3-trifluoromethylbenzyl, 3,5-bis-trifluoromethylbenzyloxy, 4-trifluoromethylphenoxy, 3-trifluoromethylphenoxy, 3-trifluoromethylphenyl, 2,3,4-trifluorophenoxy, 2,3,5-trifluorophenoxy, 3,4,5-trimethylphenoxy, 3-difluoromethoxyphenoxy, 3-pentafluoroethylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy) phenoxy, 3-trifluoromethylthiophenoxy, 3-trifluoromethylthiobenzyloxy, and trifluoromethylthio;

R_6 and R_{11} are independently selected from the group consisting of chloro, fluoro, hydrido, pentafluoroethyl, 1,1,2,2-tetrafluoroethoxy, and trifluoromethyl;

R_7 and R_{12} are independently selected from the group consisting of hydrido, fluoro, and trifluoromethyl.

[0029] In a most preferred embodiment of compounds of the invention

Y is methylene;

Z is covalent single bond;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido and fluoro with the proviso that there is no R_4, R_8, R_9, or R_{13} when the embodiment is a compound of Formula Cyclo I-H;

R_5 is selected from the group consisting of 5-bromo-2-fluorophenoxy, 4-chloro-3-ethylphenoxy, 2,3-dichlorophenoxy, 3,4-dichlorophenoxy, 3-difluoromethoxyphenoxy, 3,5-dimethylphenoxy, 3,4-dimethylphenoxy, 3-ethylphenoxy, 3-ethyl-5-methylphenoxy, 4-fluoro-3-methylphenoxy, 4-fluorophenoxy, 3-isopropylphenoxy, 3-methylphenoxy, 3-pentafluoroethylphenoxy, 3-tert -butylphenoxy, 3-(1,1,2,2-tetrafluoroethoxy)phenoxy, 2-(5,6,7,8-tetrahydronaphthyloxy), 3-trifluoromethoxybenzyloxy,3-trifluoromethoxyphenoxy, 3-trifluoromethylbenzyloxy, and 3-trifluoromethylthiophenoxy:

R_{10} is selected from the group consisting of cyclopentyl, 1,1,2,2-tetrafluoroethoxy, 2-furyl, 1,1-bis-trifluoromethyl-1-hydroxymethyl, isobutyl, isopropoxy, pentafluoroethyl, trifluoromethoxy, trifluoromethyl, and trifluoromethylthio;

R_6 and R_{11} are independently selected from the group consisting of fluoro and hydrido;

R_7 and R_{12} are independently selected from the group consisting of hydrido and fluoro.

DEFINITIONS

[0030] The use of generic terms in the description of the compounds are herein defined for clarity.

[0031] Standard single letter elemental symbols are used to represent specific types of atoms unless otherwise defined. The symbol "C" represents a carbon atom. The symbol "O" represents an oxygen atom. The symbol "N"

represents a nitrogen atom. The symbol "P" represents a phosphorus atom. The symbol "S" represents a sulfur atom. The symbol "H" represents a hydrogen atom. Double letter elemental symbols are used as defined for the elements of the periodical table (i.e., Cl represents chlorine, Se represents selenium, etc.).

[0032] As utilized herein, the term "alkyl", either alone or within other terms such as "haloalkyl" and "alkylthio", means an acyclic alkyl radical containing from 1 to about 10, preferably from 1 to about 8 carbon atoms and more preferably 1 to about 6 carbon atoms. Said alkyl radicals may be optionally substituted with groups as defined below. Examples of such radicals include methyl, ethyl, chloroethyl, hydroxyethyl, n-propyl, oxopropyl, isopropyl, n-butyl, cyanobutyl, isobutyl, sec-butyl, tert-butyl, pentyl, aminopentyl, iso-amyl, hexyl, octyl and the like.

[0033] The term "alkenyl" refers to an unsaturated, acyclic hydrocarbon radical in so much as it contains at least one double bond. Such alkenyl radicals contain from about 2 to about 10 carbon atoms, preferably from about 2 to about 8 carbon atoms and more preferably 2 to about 6 carbon atoms. Said alkenyl radicals may be optionally substituted with groups as defined below. Examples of suitable alkenyl radicals include propenyl, 2-chloropropenyl, buten-1-yl, isobutenyl, penten-1-yl, 2-2-methylbuten-1-yl, 3-methylbuten-1-yl, hexen-1-yl, 3-hydroxyhexen-1-yl, hepten-1-yl, and octen-1-yl, and the like.

[0034] The term "alkynyl" refers to an unsaturated, acyclic hydrocarbon radical in so much as it contains one or more triple bonds, such radicals containing about 2 to about 10 carbon atoms, preferably having from about 2 to about 8 carbon atoms and more preferably having 2 to about 6 carbon atoms. Said alkynyl radicals may be optionally substituted with groups as defined below. Examples of suitable alkynyl radicals include ethynyl, propynyl, hydroxypropynyl, butyn-1-yl, butyn-2-yl, pentyn-1-yl, pentyn-2-yl, 4-methoxypentyn-2-yl, 3-methylbutyn-1-yl, hexyn-1-yl, hexyn-2-yl, hexyn-3-yl, 3,3-dimethylbutyn-1-yl radicals and the like.

[0035] The term "hydrido" denotes a single hydrogen atom (H). This hydrido radical may be attached, for example, to an oxygen atom to form a "hydroxyl" radical, one hydrido radical may be attached to a carbon atom to form a "methine" radical (=CH-), or two hydrido radicals may be attached to a carbon atom to form a "methylene" ($-CH_2-$) radical.

[0036] The term "carbon" radical denotes a carbon atom without any covalent bonds and capable of forming four covalent bonds.

[0037] The term "cyano" radical denotes a carbon radical having three of four covalent bonds shared by a nitrogen atom.

[0038] The term "hydroxyalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with a hydroxyl as defined above. Specifically embraced are monohydroxyalkyl, dihydroxyalkyl and polyhydroxyalkyl radicals.

[0039] The term "alkanoyl" embraces radicals wherein one or more of the terminal alkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylalkyl and dicarbonylalkyl radicals. Examples of monocarbonylalkyl radicals include formyl, acetyl, and pentanoyl. Examples of dicarbonylalkyl radicals include oxalyl, malonyl, and succinyl.

[0040] The term "alkylene" radical denotes linear or branched radicals having from 1 to about 10 carbon atoms and having attachment points for two or more covalent bonds. Examples of such radicals are methylene, ethylene, ethylidene, methylethylene, and isopropylidene.

[0041] The term "alkenylene" radical denotes linear or branched radicals having from 2 to about 10 carbon atoms, at least one double bond, and having attachment points for two or more covalent bonds. Examples of such radicals are 1,1-vinylidene ($CH_2=C$), 1,2-vinylidene (-CH=CH-), and 1,4-butadienyl (-CH=CH-CH=CH-).

[0042] The term "halo" means halogens such as fluorine, chlorine, bromine or iodine atoms.

[0043] The term "haloalkyl" embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals. A monohaloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkyl radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkyl radicals are "lower haloalkyl" radicals having one to about six carbon atoms. Examples of such haloalkyl radicals include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, trifluoroethyl, pentafluoroethyl, heptafluoropropyt, difluorochtoromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl.

[0044] The term "hydroxyhaloalkyl" embraces radicals wherein any one or more of the haloalkyl carbon atoms is substituted with hydroxy as defined above. Examples of "hydroxyhaloalkyl" radicals include hexafluorohydoxypropyl.

[0045] The term "haloalkylene radical" denotes alkylene radicals wherein any one or more of the alkylene carbon atoms is substituted with halo as defined above. Dihalo alkylene radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkylene radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred haloalkylene radicals are "lower haloalkylene" radicals having one to about six carbon atoms. Examples of "haloalkylene" radicals include difluoromethylene, tetrafluoroethylene, tetrachloroethylene, alkyl substituted monofluoromethylene, and aryl substituted trifluoromethylene.

[0046] The term "haloalkenyl" denotes linear or branched radicals having from 1 to about 10 carbon atoms and having one or more double bonds wherein any one or more of the alkenyl carbon atoms is substituted with halo as defined above. Dihaloalkenyl radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhaloalkenyl radicals may have more than two of the same halo atoms or a combination of different halo radicals.

[0047] The terms "alkoxy" and "alkoxyalkyl" embrace linear or branched oxy-containing radicals each having alkyl portions of one to about ten carbon atoms, such as methoxy radical. The term "alkoxyalkyl" also embraces alkyl radicals having one or more alkoxy radicals attached to the alkyl radical, that is, to form monoalkoxyalkyl and dialkoxyalkyl radicals. More preferred alkoxy radicals are "lower alkoxy" radicals having one to six carbon atoms. Examples of such radicals include methoxy, ethoxy, propoxy, butoxy, isopropoxy and *tert*-butoxy alkyls. The "alkoxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkoxy" and "haloalkoxyalkyl" radicals. Examples of such haloalkoxy radicals include fluoromethoxy, chloromethoxy, trifluoromethoxy, difluoromethoxy, trifluoroethoxy, fluoroethoxy, tetrafluoroethoxy, pentafluoroethoxy, and fluoropropoxy. Examples of such haloalkoxyalkyl radicals include fluoromethoxymethyl, chloromethoxyethyl, trifluoromethoxymethyl, difluoromethoxyethyl, and trifluoroethoxymethyl.

[0048] The terms "alkenyloxy" and "alkenyloxyalkyl" embrace linear or branched oxy-containing radicals each having alkenyl portions of two to about ten carbon atoms, such as ethenyloxy or propenyloxy radical. The term "alkenyloxyalkyl" also embraces alkenyl radicals having one or more alkenyloxy radicals attached to the alkyl radical, that is, to form monoalkenyloxyalkyl and dialkenyloxyalkyl radicals. More preferred alkenyloxy radicals are "lower alkenyloxy" radicals having two to six carbon atoms. Examples of such radicals include ethenyloxy, propenyloxy, butenyloxy, and isopropenyloxy alkyls. The "alkenyloxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkenyloxy" radicals. Examples of such radicals include trifluoroethenyloxy, fluoroethenyloxy, difluoroethenyhloxy, and fluoropropenyloxy.

[0049] The term "haloalkoxyalkyl" also embraces alkyl radicals having one or more haloalkoxy radicals attached to the alkyl radical, that is, to form monohaloalkoxyalkyl and dihaloalkexyalkyl radicals. The term "haloalkenyloxy" also embraces oxygen radicals having one or more haloalkenyloxy radicals attached to the oxygen radical, that is, to form monohaloalkenyloxy and dihaloalkenyloxy radicals. The term "haloalkenyloxyalkyl" also embraces alkyl radicals having one or more haloalkenyloxy radicals attached to the alkyl radical, that is, to form monohaloalkenyloxyalkyl and dihaloalkenyloxyalkyl radicals.

[0050] The term "alkylenedioxy" radicals denotes alkylene radicals having at least two oxygens bonded to a single alkylene group. Examples of "alkylenedioxy" radicals include methylenedioxy, ethylenedioxy, alkylsubstituted methylenedioxy, and arylsubstituted methylenedioxy. The term "haloalkylenedioxy" radicals denotes haloalkylene radicals having at least two oxy groups bonded to a single haloalkyl group. Examples of "haloalkylenedioxy" radicals include difluoromethylenedioxy, tetrafluoroethylenedioxy, tetrachloroethylenedioxy, alkylsubstituted monofluoromethylenedioxy, and arylsubstituted monofluoromethylenedioxy.

[0051] The term "aryl", alone or in combination, means a carbocyclic aromatic system containing one, two or three rings wherein such rings may be attached together in a pendant manner or may be fused. The term "fused" means that a second ring is present (ie, attached or formed) by having two adjacent atoms in common (ie, shared) with the first ring. The term "fused" is equivalent to the term "condensed". The term "aryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane and biphenyl.

[0052] The term "perhaloaryl" embraces aromatic radicals such as phenyl, naphthyl, tetrahydronaphthyl, indane and biphenyl wherein the aryl radical is substituted with 3 or more halo radicals as defined below.

[0053] The term "heterocyclyl" embraces saturated, partially saturated and unsaturated heteroatom-containing ring-shaped radicals having from 5 through 15 ring members selected from carbon, nitrogen, sulfur and oxygen, wherein at least one ring atom is a heteroatom. Heterocyclyl radicals may contain one, two or three rings wherein such rings may be attached in a pendant manner or may be fused. Examples of saturated heterocyclic radicals include saturated 3 to 6-membered heteromonocylic group containing 1 to 4 nitrogen atoms[e.g. pyrrolidinyl, imidazolidinyl, piperidino, piperazinyl, etc.]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl, etc.]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl, etc.]. Examples of partially saturated heterocyclyl radicals include dihydrothiophene, dihydropyran, dihydrofuran and dihydrothiazole. Examples of unsaturated heterocyclic radicals, also termed "heteroaryl" radicals, include unsaturated 5 to 6 membered heteromonocyclyl group containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.] tetrazolyl [e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.], etc.: unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo [1,5-b]pyridazinyl, etc.], etc.; unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, 2-furyl, 3-furyl, etc.; unsaturated 5 to 6-membered heteromonocyclic group containing a sulfur atom,

for example, 2-thienyl, 3-thienyl, etc.; unsaturated 5- to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl. 1,2,5-oxadiazolyl, etc.] etc.; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzoxazolyl, benzoxadiazolyl, etc.]; unsaturated 5 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1.2.4- thiadiazolyl, 1,3,4-thiadiazolyl, 1.2.5-thiadiazolyl, etc.] etc.; unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.] and the like. The term also embraces radicals where heterocyclic radicals are fused with aryl radicals. Examples of such fused bicyclic radicals include benzofuran, benzothiophene, and the like. Said "heterocyclyl" group may have 1 to 3 substituents as defined below. Preferred heterocyclic radicals include five to twelve membered fused or unfused radicals. Non-limiting examples of heterocyclic radicals include pyrrolyl, pyridinyl, pyridyloxy, pyrazolyl, triazolyl, pyrimidinyl, pyridazinyl, oxazolyl, thiazolyl, imidazolyl, indolyl, thiophenyl, furanyl, tetrazolyl, 2-pyrrolinyl, 3-pyrrolinyl, pyrrolindinyl, 1,3-dioxolanyl, 2-imidazolinyl, imidazolidinyl, 2-pyrazolinyl, pyrazolidinyl, isoxazolyl, isothiazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, 2H-pyranyl, 4H-pyranyl, piperidinyl, 1,4-dioxanyl, morpholinyl, 1,4-dithianyl, thiomorpholinyl, pyrazinyl, piperazinyl, 1.3.5-triazinyl, 1,3,5-trithianyl, benzo(b)thiophenyl, benzimidazoyl, quinolinyl, tetraazolyl, and the like.

[0054] The term "sulfonyl", whether used alone or linked to other terms such as alkylsulfonyl, denotes respectively divalent radicals $-SO_2-$. "Alkylsulfonyl", embraces alkyl radicals attached to a sulfonyl radical, where alkyl is defined as above. "Alkylsulfonylalkyl", embraces alkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. "Haloalkylsulfonyl", embraces haloalkyl radicals attached to a sulfonyl radical, where haloalkyl is defined as above. "Haloalkylsulfonylalkyl", embraces haloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "aminosulfonyl" denotes an amino radical attached to a sulfonyl radical.

[0055] The term "sulfinyl", whether used alone or linked to other terms such as alkylsulfinyl, denotes respectively divalent radicals -S(O)-. "Alkylsulfinyl", embraces alkyl radicals attached to a sulfinyl radical, where alkyl is defined as above. "Alkylsulfinylalkyl", embraces alkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above. "Haloalkylsulfinyl", embraces haloalkyl radicals attached to a sulfinyl radical, where haloalkyl is defined as above. "Haloalkylsulfinylalkyl", embraces haloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above.

[0056] The term "aralkyl" embraces aryl-substituted alkyl radicals. Preferable aralkyl radicals are "lower aralkyl" radicals having aryl radicals attached to alkyl radicals having one to six carbon atoms. Examples of such radicals include benzyl, diphenylmethyl, triphenylmethyl, phenylethyl and diphenylethyl. The terms benzyl and phenylmethyl are interchangeable.

[0057] The term "heteroaralkyl" embraces heteroaryl-substituted alkyl radicals wherein the heteroaralkyl radical may be additionally substituted with three or more substituents as defined above for aralkyl radicals. The term "perhaloaralkyl" embraces aryl-substituted alkyl radicals wherein the aralkyl radical is substituted with three or more halo radicals as defined above.

[0058] The term "aralkylsulfinyl", embraces aralkyl radicals attached to a sulfinyl radical, where aralkyl is defined as above. "Aralkylsulfinylalkyl", embraces aralkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above.

[0059] The term "aralkylsulfonyl", embraces aralkyl radicals attached to a sulfonyl radical, where aralkyl is defined as above. "Aralkylsulfonylalkyl", embraces aralkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

[0060] The term "cycloalkyl" embraces radicals having three to ten carbon atoms. More preferred cycloalkyl radicals are "lower cycloalkyl" radicals having three to seven carbon atoms. Examples include radicals such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. The term "cycloalkylalkyl" embraces cycloalkyl-substituted alkyl radicals. Preferable cycloalkylalkyl radicals are "lower cycloalkylalkyl" radicals having cycloalkyl radicals attached to alkyl radicals having one to six carbon atoms. Examples of such radicals include cyclohexylhexyl. The term "cycloalkenyl" embraces radicals having three to ten carbon atoms and one or more carbon-carbon double bonds. Preferred cycloalkenyl radicals are "lower cycloalkenyl" radicals having three to seven carbon atoms. Examples include radicals such as cyclobutenyl, cyclopentenyl, cyclohexenyl and cycloheptenyl. The term "halocycloalkyl" embraces radicals wherein any one or more of the cycloalkyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkyl, dihalocycloalkyl and polyhalocycloalkyl radicals. A monohalocycloalkyl radical, for one example, may have either a bromo. chloro or a fluoro atom within the radical. Dihalo radicals may have two or more of the same halo atoms or a combination of different halo radicals and polyhalocycloalkyl radicals may have more than two of the same halo atoms or a combination of different halo radicals. More preferred halocycloalkyl radicals are "lower halocycloalkyl" radicals having three to about eight carbon atoms. Examples of such halocycloalkyl radicals include fluorocyclopropyl, difluorocyclobutyl, trifluorocyclopentyl, tetrafluorocyclohexyl, and dichlorocyclopropyl. The term "halocycloalkenyl" embraces radicals wherein any one or more of the cycloalkenyl carbon atoms is substituted with halo as defined above. Specifically embraced are monohalocycloalkenyl, dihalocycloalkenyl and polyhalocycloalkenyl radicals.

[0061] The term "cycloalkoxy" embraces cycloalkyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexoxy and cyclopentoxy. The term "cycloalkoxyalkyl" also embraces alkyl radicals having one or more cycloalkoxy radicals attached to the alkyl radical, that is, to form monocycloalkoxyalkyl and dicycloalkoxyalkyl radicals. Examples of such radicals include cyclohexoxyethyl. The "cycloalkoxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "halocycloalkoxy" and "halocycloalkoxyalkyl" radicals.

[0062] The term "cycloalkylalkoxy" embraces cycloalkyl radicals attached to an alkoxy radical. Examples of such radicals includes cyclohexylmethoxy and cyclopentylmethoxy.

[0063] The term "cycloalkenyloxy" embraces cycloalkenyl radicals attached to an oxy radical. Examples of such radicals includes cyclohexenyloxy and cyclopentenyloxy. The term "cycloalkenyloxyalkyl" also embraces alkyl radicals having one or more cycloalkenyloxy radicals attached to the alkyl radical, that is, to form monocycloalkenyloxyalkyl and dicycloalkenyloxyalkyl radicals. Examples of such radicals include cyclohexenyloxyethyl. The "cycloalkenyloxy" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "halocycloalkenyloxy" and "halocycloalkenyloxyalkyl" radicals.

[0064] The term "cycloalkylenedioxy" radicals denotes cycloalkylene radicals having at least two oxygens bonded to a single cycloalkylene group. Examples of "alkylenedioxy" radicals include 1,2-dioxycyclohexylene.

[0065] The term "cycloalkylsulfinyl ", embraces cycloalkyl radicals attached to a sulfinyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfinylalkyl", embraces cycloalkylsulfinyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "Cycloalkylsulfonyl", embraces cycloalkyl radicals attached to a sulfonyl radical, where cycloalkyl is defined as above. "Cycloalkylsulfonylalkyl", embraces cycloalkylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

[0066] The term "cycloalkylalkanoyl" embraces radicals wherein one or more of the cycloalkyl carbon atoms are substituted with one or more carbonyl radicals as defined below. Specifically embraced are monocarbonylcycloalkyl and dicarbonylcycloalkyl radicals. Examples of monocarbonylcycloalkyl radicals include cyclohexylcarbonyl, cyclohexylacetyl, and cyclopentylcarbonyl. Examples of dicarbonylcycloalkyl radicals include 1,2-dicarbonylcyclohexane.

[0067] The term "alkylthio" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, attached to a divalent sulfur atom. More preferred alkylthio radicals are "lower alkylthio" radicals having one to six carbon atoms. An example of "lower alkylthio" is methylthio (CH_3-S-). The "alkylthio" radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkylthio" radicals. Examples of such radicals include fluoromethylthio, chloromethylthio, trifluoromethylthio, difluoromethylthio, trifluoroethylthio, fluoroethylthio, tetrafluoroethylthio, pentafluoroethylthio, and fluoropropylthio.

[0068] The term "alkyl aryl amino" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, and one aryl radical both attached to an amino radical. Examples include N-methyl-4-methoxyaniline. N-ethyl-4-methoxyaniline, and N-methyl-4-trifluoromethoxyaniline.

[0069] The terms alkylamino denotes "monoalkylamino" and "dialkylamino" containing one or two alkyl radicals, respectively, attached to an amino radical.

[0070] The terms arylamino denotes "monoarylamino" and "diarylamino" containing one or two aryl radicals, respectively, attached to an amino radical. Examples of such radicals include N-phenylamino and N-naphthylamino.

[0071] The term "aralkylamino", embraces aralkyl radicals attached to an amino radical, where aralkyl is defined as above. The term aralkylamino denotes "monoaralkylamino" and "diaralkylamino" containing one or two aralkyl radicals, respectively, attached to an amino radical. The term aralkylamino further denotes "monoaralkyl monoalkylamino" containing one aralkyl radical and one alkyl radical attached to an amino radical.

[0072] The term "arylsulfinyl" embraces radicals containing an aryl radical, as defined above, attached to a divalent S(=O) atom. The term "arylsulfinylalkyl" denotes arylsulfinyl radicals attached to a linear or branched alkyl radical, of one to ten carbon atoms.

[0073] The term "arylsulfonyl", embraces aryl radicals attached to a sulfonyl radical, where aryl is defined as above, "arylsulfonylalkyl", embraces arylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above. The term "heteroarylsulfinyl" embraces radicals containing an heteroaryl radical, as defined above, attached to a divalent S(=O) atom. The term "heteroarylsulfinylalkyl" denotes heteroarylsulfinyl radicals attached to a linear or branched alkyl radical, of one to ten carbon atoms. The term "Heteroarylsulfonyl", embraces heteroaryl radicals attached to a sulfonyl radical, where heteroaryl is defined as above. "Heteroarylsulfonylalkyl", embraces heteroarylsulfonyl radicals attached to an alkyl radical, where alkyl is defined as above.

[0074] The term "aryloxy" embraces aryl radicals, as defined above, attached to an oxygen atom. Examples of such radicals include phenoxy, 4-chloro-3-ethylphenoxy, 4-chloro-3-methylphenoxy, 3-chloro-4-ethylphenoxy, 3,4-dichlorophenoxy, 4-methylphenoxy, 3-trifluoromethoxyphenoxy, 3-trifluoromethylphenoxy, 4-fluorophenoxy, 3,4-dimethylphenoxy, 5-bromo-2-fluorophenoxy, 4-bromo-3-fluorophenoxy, 4-fluoro-3-methylphenoxy, 5,6,7,8-tetrahydronaphthyloxy, 3-isopropylphenoxy, 3-cyclopropylphenoxy, 3-ethylphenoxy, 4-*tert*-butylphenoxy, 3-pentafluoroethylphenoxy, and 3-(1,1,2,2-tetrafluoroethoxy)phenoxy.

[0075] The term "aroyl" embraces aryl radicals, as defined above, attached to an carbonyl radical as defined above.

Examples of such radicals include benzoyl and toluoyl.

[0076] The term "aralkanoyl" embraces aralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, phenylacetyl.

[0077] The term "aralkoxy" embraces oxy-containing aralkyl radicals attached through an oxygen atom to other radicals. More preferred aralkoxy radicals are "lower aralkoxy" radicals having phenyl radicals attached to lower alkoxy radical as described above. Examples of such radicals include benzyloxy, 1-phenylethoxy, 3-trifluoromethoxybenzyloxy, 3-trifluoromethylbenzyloxy, 3,5-difluorobenyloxy, 3-bromobenzyloxy, 4-propylbenzyloxy, 2-fluoro-3-trifluoromethylbenzyloxy, and 2-phenylethoxy.

[0078] The term "aryloxyalkyl" embraces aryloxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include phenoxymethyl.

[0079] The term "haloaryloxyalkyl" embraces aryloxyalkyl radicals, as defined above, wherein one to five halo radicals are attached to an aryloxy group.

[0080] The term "heteroaroyl" embraces heteroaryl radicals, as defined above, attached to an carbonyl radical as defined above. Examples of such radicals include furoyl and nicotinyl.

[0081] The term "heteroaralkanoyl" embraces heteroaralkyl radicals, as defined herein, attached to an carbonyl radical as defined above. Examples of such radicals include, for example, pyridylacetyl and furylbutyryl.

[0082] The term "heteroaralkoxy" embraces oxy-containing heteroaralkyl radicals attached through an oxygen atom to other radicals. More preferred heteroaralkoxy radicals are "lower heteroaralkoxy" radicals having heteroaryl radicals attached to lower alkoxy radical as described above.

[0083] The term "haloheteroaryloxyalkyl" embraces heteroaryloxyalkyl radicals, as defined above, wherein one to four halo radicals are attached to an heteroaryloxy group.

[0084] The term "heteroarylamino" embraces heterocyclyl radicals, as defined above, attached to an amino group. Examples of such radicals include pyridylamino.

[0085] The term "heteroarylaminoalkyl" embraces heteroarylamino radicals, as defined above, attached to an alkyl group. Examples of such radicals include pyridylmethylamino.

[0086] The term "heteroaryloxy" embraces heterocyclyl radicals, as defined above, attached to an oxy group. Examples of such radicals include 2-thiophenyloxy, 2-pyrimidyloxy, 2-pyridyloxy, 3-pyridyloxy, and 4-pyridyloxy.

[0087] The term "heteroaryloxyalkyl" embraces heteroaryloxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include 2-pyridyloxymethyl, 3-pyridyloxyethyl, and 4-pyridyloxymethyl.

[0088] The term "arylthio" embraces aryl radicals, as defined above, attached to an sulfur atom. Examples of such radicals include phenylthio.

[0089] The term "arylthioalkyl" embraces arylthio radicals, as defined above, attached to an alkyl group. Examples of such radicals include phenylthiomethyl.

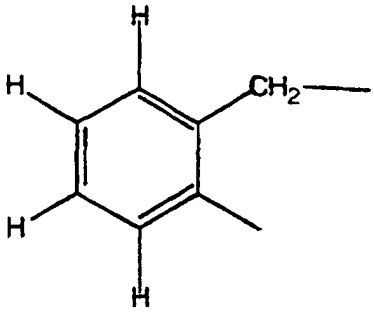
[0090] The term "alkylthioalkyl" embraces alkylthio radicals, as defined above, attached to an alkyl group. Examples of such radicals include methylthiomethyl. The term "alkoxyalkyl" embraces alkoxy radicals, as defined above, attached to an alkyl group. Examples of such radicals include methoxymethyl.

[0091] The term "carbonyl" denotes a carbon radical having two of the four covalent bonds shared with an oxygen atom. The term "carboxy" embraces a hydroxyl radical, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "carboxamide" embraces amino, monoalkylamino, dialkylamino, monocycloalkylamino, alkylcycloalkylamino, and dicycloalkylamino radicals, attached to one of two unshared bonds in a carbonyl group. The term "carboxamidoalkyl" embraces carboxamide radicals, as defined above, attached to an alkyl group. The term "carboxyalkyl" embraces a carboxy radical, as defined above, attached to an alkyl group. The term "carboalkoxy" embraces alkoxy radicals, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "carboaralkoxy" embraces aralkoxy radicals, as defined above, attached to one of two unshared bonds in a carbonyl group. The term "monocarboalkoxyalkyl" embraces one carboalkoxy radical, as defined above, attached to an alkyl group. The term "dicarboalkoxyalkyl" embraces two carboalkoxy radicals, as defined above, attached to an alkylene group. The term "monocyanoalkyl" embraces one cyano radical, as defined above, attached to an alkyl group. The term "dicyanoalkylene" embraces two cyano radicals, as defined above, attached to an alkyl group. The term "carboalkoxycyanoalkyl" embraces one cyano radical, as defined above, attached to an carboalkoxyalkyl group.

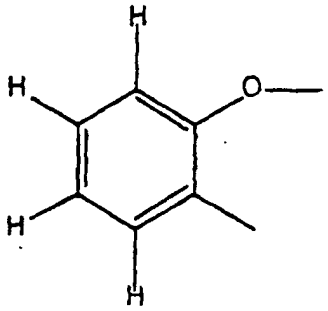
[0092] The term "acyl", alone or in combination, means a carbonyl or thionocarbonyl group bonded to a radical selected from, for example, hydrido, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, alkoxyalkyl, haloalkoxy, aryl, heterocyclyl, heteroaryl, alkylsulfinylalkyl, alkylsulfonylalkyl, aralkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, alkylthio, arylthio, amino, alkylamino, dialkylamino, aralkoxy, arylthio, and alkylthioalkyl. Examples of "acyl" are formyl, acetyl, benzoyl, trifluoroacetyl, phthaloyl, malonyl, nicotinyl, and the like. The term "haloalkanoyl" embraces one or more halo radicals, as defined herein, attached to an alkanoyl radical as defined above. Examples of such radicals include, for example, chloroacetyl, trifluoroacetyl, bromopropanoyl, and heptafluorobutanoyl. The term "diacyl", alone or in combination, means having two or more carbonyl or thionocarbonyl groups bonded to a radical selected from, for example. alkylene, alkenylene, alkynylene, haloalkylene, alkoxyalkylene, aryl, heterocyclyl, heteroaryl, aralkyl, cycloalkyl, cycloalkylalkyl,

and cycloalkenyl. Examples of "diacyl" are phthaloyl, malonyl, succinyl, adipoyl, and the like.

[0093] The term "benzylidenyl" radical denotes substituted and unsubstituted benzyl groups having attachment points for two covalent bonds. One attachment point is through the methylene of the benzyl group with the other attachment point through an ortho carbon of the phenyl ring. The methylene group is designated for attached to the lowest numbered position. Examples include the base compound benzylidene of structure:



[0094] The term "phenoxylidenyl" radical denotes substituted and unsubstituted phenoxy groups having attachment points for two covalent bonds. One attachment point is through the oxy of the phenoxy group with the other attachment point through an ortho carbon of the phenyl ring. The oxy group is designated for attached to the lowest numbered position. Examples include the base compound phenoxylidene of structure:



[0095] The term "phosphono" embraces a pentavalent phosphorus attached with two covalent bonds to an oxygen radical. The term "dialkoxyphosphono" denotes two alkoxy radicals, as defined above, attached to a phosphono radical with two covalent bonds. The term "diaralkoxyphosphono" denotes two aralkoxy radicals, as defined above, attached to a phosphono radical with two covalent bonds. The term "dialkoxyphosphonoalkyl" denotes dialkoxyphosphono radicals, as defined above, attached to an alkyl radical. The term "diaralkoxyphosphonoalkyl" denotes diaralkoxyphosphono radicals, as defined above, attached to an alkyl radical.

[0096] Said "alkyl", "alkenyl", "alkynyl", "alkanoyl", "alkylene", "alkenylene", "benzylidenyl", "phenoxylidenyl", "hydroxyalkyl", "haloalkyl", "haloalkylene", "haloalkenyl", "alkoxy", "alkenyloxy", "alkenyloxyalkyl", "alkoxyalkyl", "aryl", "perhaloaryl", "haloalkoxy", "haloalkoxyalkyl", "haloalkenyloxy", "haloalkenyloxyalkyl", "alkylenedioxy", "haloalkylenedioxy", "heterocyclyl", "heteroaryl", "hydroxyhaloalkyl", "alkylsulfonyl", "haloalkylsulfonyl", "alkylsulfonylalkyl", "haloalkylsulfonylalkyl", "alkylsulfinyl", "alkylsulfinylalkyl", "haloalkylsulfinylalkyl", "aralkyl", "heteroaralkyl", "perhaloaralkyl", "aralkylsulfonyl", "aralkylsulfonylalkyl", "aralkylsulfinyl", "aralkylsulfinylalkyl", "cycloalkyl", "cycloalkylalkanoyl", "cycloalkylalkyl", "cycloalkenyl", "halocycloalkyl", "halocycloalkenyl", "cycloalkylsulfinyl", "cycloalkylsulfinylalkyl", "cycloalkylsulfonyl", "cycloalkylsulfonylalkyl", "cycloalkoxy", "cycloalkoxyalkyl", "cycloalkylalkoxy", "cycloalkenyloxy", "cycloalkenyloxyalkyl", "cycloalkylenedioxy", "halocycloalkoxy", "halocycloalkoxyalkyl", "halocycloalkenyloxy", "halocycloalkenyloxyalkyl", "alkylthio", "haloalkylthio", "alkylsulfinyl", "amino", "oxy", "thio", "alkylamino", "arylamino", "aralkylamino", "arylsulfinyl", "arylsulfinylalkyl", "arylsulfonyl", "arylsulfonylalkyl", "heteroarylsulfinyl", "heteroarylsulfinylalkyl", "heteroarylsulfonyl", "heteroarylsulfonylalkyl", "heteroarylamino", "heteroarylaminoalkyl", "heteroaryloxy", "heteroaryloxylalkyl", "aryloxy", "aroyl", "aralkanoyl", "aralkoxy", "aryloxyalkyl", "haloaryloxyalkyl", "heteroaroyl", "heteroaralkanoyl", "heteroaralkoxy", "heteroaralkoxyalkyl", "arylthio", "arylthioalkyl", "alkoxyalkyl", "acyl" and "diacyl" groups defined above may optionally have 1 to 5 non-hydrido substituents such as perhaloaralkyl, aralkylsulfonyl, aralkylsul-

fonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, heteroaryloxy, heteroaryloxylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarbonyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl,

[0097] The term "spacer" can include a covalent bond and a linear moiety having a backbone of 1 to 7 continous atoms. The spacer may have 1 to 7 atoms of a univalent or multi-valent chain. Univalent chains may be constituted by a radical selected from =C(H)-, =C(R_{17})-, -O-, -S-, -S(O)-, -S($O)_2$-, -NH-, -N(R_{17})-, -N=, -CH(OH)-, =C(OH)-, -CH(OR_{17})-, =C(OR_{17})-, and -C(O)- wherein R_{17} is selected from alkyl, alkenyl, alkynyl, aryl, heteroaryl, aralkyl, aryloxyalkyl, alkoxyalkyl, alkylthioalkyl, arylthioalkyl, cycloalkyl, cycloalkylalkyl, haloalkyl, haloalkenyl, haloalkoxyalkyl, perhaloaralkyl, heteroarylalkyl, heteroaryloxyalkyl, heteroarylthioalkyl, and heteroarylalkenyl. Multi-valent chains may consist of a straight chain of 1 or 2 or 3 or 4 or 5 or 6 or 7 atoms or a straight chain of 1 or 2 or 3 or 4 or 5 or 6 atoms with a side chain. The chain may be constituted of one or more radicals selected from: lower alkylene, lower alkenyl, -O-, -O-CH_2-, -S-CH_2-. -CH_2CH_2-, ethenyl, -CH=CH(OH)-, -OCH_2O-, -$O(CH_2)_2O$-, -$NHCH_2$-, -OCH(R_{17})O-, -O(CH_2CHR_{17})O-, -OCF_2O-, -$O(CF_2)_2O$-, -S-, -S(O)-, -S($O)_2$-, -N(H)-, -N(H)O-, -N(R_{17})O-, -N(R_{17})-, -C(O)-, -C(O)NH-, -C(O)NR_{17}-, -N=, -OCH_2-, -SCH_2-, S(O)CH_2-, -$CH_2C(O)$-, -CH(OH)-, =C(OH)-, -CH(OR_{17})-, =C(OR_{17})-, S($O)_2CH_2$-, and -N$R_{17}CH_2$- and many other radicals defined above or generally known or ascertained by one of skill-in-the art. Side chains may include substituents such as 1 to 5 non-hydrido substituents such as perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, heteroaryloxy, heteroaryloxylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, cycloalkylenedioxy, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, lower alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, monoarylamidosulfonyl, arylsulfonamido, diarylamidosulfonyl, monoalkyl monoaryl amidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, alkylenedioxy, haloalkylenedioxy, cycloalkyl, cycloalkenyl, lower cycloalkylalkyl, lower cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, arylalkyl, heteroarylalkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl.

[0098] Chiral compounds of the present invention have a hydroxyl group substitutent on a chiral carbon of the alkanol and propanol compounds of the present invention specifically in the R-stereoisomeric configuration based on the Cahn-Ingold-Prelog convention for stereoisomeric carbon atoms. The R-stereoisomeric configuration compounds of the present invention may optionally have one or more additional chiral carbons present in each compound. The R-stereoisomeric configuration compounds of the present invention can exist in tautomeric, geometric, and other stereoisomeric forms. The present invention having a hydroxyl group substitutent on a chiral carbon of the alkanol and propanol compounds in the R-stereoisomeric configuration contemplates all such forms of said invented compounds, including cis- and trans-geometric isomers, E- and Z-geometric isomers, diastereomers, and other mixtures thereof, as falling within the scope of the invention. Pharmaceutically acceptable sales of such tautomeric, geometric or stereoisomeric forms are also included within the invention. The standard definitions for the Cahn-Ingold-Prelog convention and stereochemical system can be found in Pure Applied Chemistry, 1976, Vol. 45, pages 15-30 and Cahn et al., Angewandte

Chemie International Edition English, 1966, Vol. 5, pages 385-415.

[0099] The terms "cis" and "trans" denote a form of geometric isomerism in which two carbon atoms connected by a double bond will each have a hydrogen atom on the same side of the double bond ("cis") or on opposite sides of the double bond ("trans").

[0100] Some of the compounds described contain alkenyl groups, and are meant to include both cis and trans or "E" and "Z" geometric forms.

[0101] Some of the compounds described contain one or more stereocenters in addition to said hydroxyl group substitutent on a chiral carbon of the alkanol and propanol compounds in the R-stereoisomeric configuration and are meant to include R, S, and mixtures of R and S forms for each additional stereocenter present.

[0102] Some of the compounds described herein may contain one or more ketonic or aldehydic carbonyl groups or combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or principally in the "keto" form and in part or principally as one or more "enol" forms of each aldehyde and ketone group present. Compounds of the present invention having aldehydic or ketonic carbonyl groups are meant to include both "keto" and "enol" tautomeric forms.

[0103] Some of the compounds described herein may contain one or more amide carbonyl groups or combinations thereof alone or as part of a heterocyclic ring system. Such carbonyl groups may exist in part or principally in the "keto" form and in part or principally as one or more "enol" forms of each amide group present. Compounds of the present invention having amidic carbonyl groups are meant to include both "keto" and "enol" tautomeric forms. Said amide carbonyl groups may be both oxo (C=O) and thiono (C=S) in type.

[0104] Some of the compounds described herein may contain one or more imine or enamine groups or combinations thereof. Such groups may exist in part or principally in the "imine" form and in part or principally as one or more "enamine" forms of each group present. Compounds of the present invention having said imine or enamine groups are meant to include both "imine" and "enamine" tautomeric forms.

[0105] The following general synthetic sequences are useful in making the present invention. Abbreviations used in the schemes are as follows: "AA" represents amino acids, "BINAP" represents 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, "Boc" represents tert-butyloxycarbonyl, "BOP" represents benzotriazol-1-yl-oxy-tris-(dimethylamino), "bu" represents butyl, "dba" represents dibenzylideneacetone, "DCC" represents 1,3-dicyclohexylcarbodiimide, "DIBAH" represents diisobutylaluminum hydride, "DIPEA" represents diisopropylethylamine, "DMF" represents dimethylformamide, "DMSO" represents dimethylsulfoxide. "Fmoc" represents 9-fluorenylmethoxycarbonyl, "LDA" represents lithium diisopropylamide, "PHTH" represents a phthaloyl group, "pnZ" represents 4-nitrobenzyloxycarbonyl, "PTC" represents a phase transfer catalyst, "p-TsOH" represents paratoluenesulfonic acid, "TBAF" represents tetrabutylammonium fluoride, "TBTU" represents 2-(1H-benzotriozole-1-yl)-1,1,3,3-tetramethyl uronium tetrafluoroborate. "TEA" represents triethylamine, "TFA" represents trifluoroacetic acid, "THF" represents tetrahydrofuran, "TMS" represents trimethylsilyl, and "Z" represents benzyloxycarbonyl.

[0106] The present invention comprises a pharmaceutical composition comprising a therapeutically-effective amount of a compound of Formula M together with a pharmaceutically-acceptable carrier.

[0107] The present invention also comprises the use of a compound of Formula M or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment or prophylaxis of coronary artery disease and other CETP-mediated disorders in a subject.

[0108] Compounds of the invention are capable of inhibiting activity of cholesteryl ester transfer protein (CETP), and thus could be used in the manufacture of a medicament, a method for the prophylactic or therapeutic treatment of diseases mediated by CETP, such as peripheral vascular disease, hyperlipidaemia, hypercholesterolemia, and other diseases attributable to either high LDL and low HDL or a combination of both, or a procedure to study the mechanism of action of the cholesteryl ester transfer protein (CETP) to enable the design of better inhibitors. The compounds of the invention would be also useful in prevention of cerebral vascular accident (CV A) or stroke.

[0109] Also included in the family of compounds of the invention are the pharmaceutically-acceptable salts thereof. The term "pharmaceutically-acceptable salts" embraces salts commonly used to form alkali metal salts and to form addition salts of free acids or free bases. The nature of the salt is not critical, provided that it is pharmaceutically acceptable. Suitable pharmaceutically-acceptable acid addition salts of compounds of the invention may be prepared from inorganic acid or from an organic acid. Examples of such inorganic acids are hydrochloric, hydrobromic, hydroiodic, nitric, carbonic, sulfuric and phosphoric acid. Appropriate organic acids may be selected from aliphatic, cycloaliphatic, aromatic, araliphatic, heterocyclic, carboxylic and sulfonic classes of organic acids, examples of which are formic, acetic, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, ascorbic, glucoronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, anthranilic, mesylic, salicylic, p-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, ethylsulfonic, benzenesulfonic, sulfanilic, stearic, cyclohexylaminosulfonic, algenic, galacturonic acid. Suitable pharmaceutically-acceptable base addition salts of compounds of the invention include metallic salts made from aluminum, calcium, lithium, magnesium, potassium, sodium and zinc or organic salts made from N,N'-dibenzylethyleneldiamine, choline, chloroprocaine, diethanolamine, ethylenediamine, meglumine (N-methylglu-

camine) and procain. All of these salts may be prepared by conventional means from the corresponding compound of the invention by reacting, for example, the appropriate acid or base with the compound of the invention.

[0110] Also embraced within this invention is a class of pharmaceutical composition comprising the active compounds of the invention in association with one or more non-toxic, pharmaceutically-acceptabie carriers and/or diluents and/or adjuvants (collectively referred to herein as "carrier" materials) and, if desired, other active ingredients. The active compounds of the present invention may be administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. The active compounds and composition may, for example, be administered orally, intravascularly, intraperitoneally, subcutaneously, intramuscularly or topically.

[0111] For oral administration, the pharmaceutical composition may be in the form of, for example, a tablet, capsule, suspension or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. Examples of such dosage units are tablets or capsules. The active ingredient may also be administered by injection as a composition wherein, for example, saline, dextrose or water may be used as a suitable carrier.

[0112] The amount of therapeutically active compounds which are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the disease, the route and frequency of administration, and the particular compound employed, and thus may vary widely.

[0113] The pharmaceutical compositions may contain active ingredients in the range of about 0.1 to 2000 mg, and preferably in the range of about 0.5 to 500 mg. A daily dose of about 0.01 to 100 mg/kg body weight, and preferably between about 0.5 and about 20 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day.

[0114] The compounds may be formulated in topical ointment or cream, or as a suppository, containing the active ingredients in a total amount of, for example, 0.075 to 30% w/w, preferably 0.2 to 20% w/w and most preferably 0.4 to 15% w/w. When formulated in an ointment. the active ingredients may be employed with either paraffinic or a water-miscible ointment base. Alternatively, the active ingredients may be formulated in a cream with an oil-in-water cream base. If desired, the aqueous phase of the cream base may include, for example at least 30% w/w of a polyhydric alcohol such as propylene glycol, butane-1,3-diol, mannitol, sorbitol, glycerol, polyethylene glycol and mixtures thereof. The topical formulation may desirably include a compound which enhances absorption or penetration of the active ingredient through the skin or other affected areas. Examples of such dermal penetration enhancers include dimethylsulfoxide and related analogs. The compounds of this invention can also be administered by a transdermal device. Preferably topical administration will be accomplished using a patch either of the reservoir and porous membrane type or of a solid matrix variety. In either case, the active agent is delivered continuously from the reservoir or microcapsules through a membrane into the active agent permeable adhesive, which is in contact with the skin or mucosa of the recipient. If the active agent is absorbed through the skin, a controlled and predetermined flow of the active agent is administered to the recipient. In the case of microcapsules, the encapsulating agent may also function as the membrane.

[0115] The oily phase of the emulsions of this invention may be constituted from known ingredients in a known manner. While the phase may comprise merely an emulsifier, it may comprise a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier which acts as a stabilizer. It is also preferred to include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make-up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base which forms the oily dispersed phase of the cream formulations. Emulsifiers and emulsion stabilizers suitable for use in the formulation of the present invention include Tween 60, Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl monostearate, and sodium lauryl sulfate, among others.

[0116] The choice of suitable oils or fats for the formulation is based on achieving the desired cosmetic properties, since the solubility of the active compound in most oils likely to be used in pharmaceutical emulsion formulations is very low. Thus, the cream should preferably be a non-greasy, non-staining and washable product with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils can be used.

[0117] For therapeutic purposes, the active compounds of this combination invention are ordinarily combined with one or more adjuvants appropriate to the indicated route of administration. If administered *per os*, the compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanoic acids, cellulose alkyl esters, talc, stearic acid, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, gelatin, acacia gum, sodium alginate, polyvinylpyrrolidone, and/or polyvinyl alcohol, and then tableted or encapsulated for convenient

administration. Such capsules or tablets may contain a controlled-release formulation as may be provided in a dispersion of active compound in hydroxypropylmethyl cellulose. Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. These solutions and suspensions may be prepared from sterile powders or granules having one or more of the carriers or diluents mentioned for use in the formulations for oral administration. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, and/or various buffers. Other adjuvants and modes of administration are well and widely known in the pharmaceutical art.

[0118] The present invention further provides a process for the preparation of (R)-chiral compounds of the invention by reacting suitable secondary amines with (R)-chiral forms of alcohols, epoxides, and cyclic sulfate esters.

[0119] The present invention also provides a process for the preparation of (R)-chiral compounds of the invention by reacting a suitable secondary amine with a substantially stoichiometric amount of a (R)-chiral epoxide in the presence of a transition metal-based salt.

[0120] The present invention also provides a process for the preparation of (R)-chiral precursor compounds useful in the preparation of compounds of the invention

by reacting a suitable primary amine with a substantially stoichiometric amount of a (R)-chiral epoxide with or without the presence of an added transition metal-based compound.

[0121] All mentioned references are incorporated by reference as if here written.

[0122] Although this invention has been described with respect to specific embodiments, the details of these embodiments are not to be construed as limitations.

GENERAL SYNTHETIC PROCEDURES

[0123] The compounds of the present invention can be synthesized, for example, according to the following procedures of Schemes through 15 below, wherein the substituents are as defined for Formulas I-H, I-C and I-CP above except where further noted.

[0124] It will be understood that the following description of synthetic procedures is applicable to the synthesis of the compounds of Formula M as well as to the broader group of compounds of Formula I-H. However, this is not intended to imply that the scope of the invention extends beyond that of the claims.

[0125] Synthetic Scheme 1 shows the preparation of compounds of formula XIIIA-H ("Secondary Heteroaryl Amines") which are intermediates in the preparation of the compounds corresponding to Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"). Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") wherein A and Q are independently aryl and heteroaryl. Schemes 1 through 3, taken together, prepare 1-substitutedamino-2-alkanols by addition of a halogenated, oxygen containing precursor to a secondary amine to introduce an oxy containing alkyl group wherein the two groups making up the secondary amine both are made up of aromatic groups or both groups contain aromatic rings wherein said aromatic rings maybe 0 to 2 aryl rings and 0 to 2 heteroaryl rings.

[0126] The "Generic Imine" corresponding to Formula XII can be prepared through dehydration techniques generally known in or adaptable from the art by reacting "Generic Amine-I" of Formula X with the "Generic Carbonyl Compound" of Formula XI in Scheme 1 and subsequent specific examples. For example, when Z is a covalent bond, methylene, methine substituted with another subsitutent, ethylene, or another subsituent as defined in Formula I-H, the two reactants (X and XI) react by refluxing them in an aprotic solvent, such as hexane, toluene, cyclohexane, benzene, and the like, using a Dean-Stark type trap to remove water. After about 2-8 hours or until the removal of water is complete, the aprotic solvent is removed *in vacuo* to yield the "Generic Imine" of Formula XII. Alternately, when Z is an oxygen, the "Generic Imine" is an oxime derivative. Alternately, when Z is a nitrogen, the "Generic Imine" is a hydrazone derivative. Hydrazone type "Generic Imine" compounds are readily prepared from the corresponding hydrazine and the appropriate aldehyde or ketone type "Generic Carbonyl Compound". Suitable procedures for forming oxime and hydrazone imines are also described by Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and by Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons, which are incorporated herein by reference.

[0127] The "Generic Secondary Amines" of Formula XIII can be prepared from the corresponding "Generic Imine" of Formula XII in several ways. For example, in one synthetic scheme (Reduction Method-1), which is preferred when Z is a nitrogen, the "Generic Imine" hydrazone of Formula XII is partially or completely dissolved in lower alkanols containing sufficient organic acid or mineral acid as described in WO Patent Application No.9738973, Swiss Patent CH 441366 and U. S. Patent Nos. 3359316 and 3334017, which are incorporated herein by reference, and then hydrogenated at 0-100°C, more preferrably 20-50°C, and most preferrably between 20-30°C and pressures of 10-200

psi hydrogen or more preferrably between 50-70 psi hydrogen in the presence of a noble metal catalyst such as PtO_2.

[0128] In another synthetic scheme (Reduction Method-2), which is preferrred when Z is a single bond or carbon, the "Generic Imine" of Formula XII is slurried in a lower alcohol such as ethanol, methanol or like solvent at 0-10°C and solid sodium borohydride is added in batches over 5-10 minutes at 0-10°C with stirring. The reaction mixture is stirred below 10°C for 30-90 minutes and then is warmed gradually to 15-30°C. After about 1-10 hours, the mixture is cooled and acid is added until the aqueous layer was just acidic (pH 5-7).

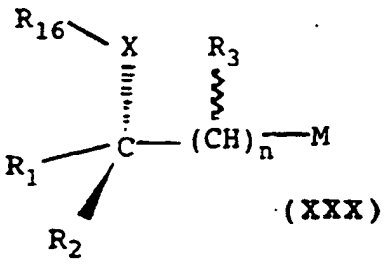
[0129] In yet another synthetic scheme (Reduction Method-3), which is preferrred when Z is an oxygen, the "Generic Imine" oxime of Formula XII is slurried in a lower alcohol solvent such methanol or like solvent at 0-10°C and acidified to a pH less than 4. Solid sodium cyanoborohydride is added in batches over 30-90 minutes at 0-20°C with stirring and addition of a suitable organic or mineral acid to keep the pH at or below 4. The reaction mixture is stirred and warmed gradually to about 20-25°C. After about 1-10 hours. the mixture is cooled and base added until the mixture was just slightly alkaline.

[0130] The "Generic Secondary Amines" of Formula XIII can also be prepared, according to Scheme 1 by an alkylation procedures based on the nucleophilic substitution of bromides by amines. In one synthetic alkylation scheme (Alkylation Method-1), a "Generic Amine-1" of Formula X is reacted with a "Generic Bromide-2" of Formula XXIII as described in Vogel's Textbook of Practical Organic Chemistry, Fifth Edition, 1989, pages 902 to 905 and references cited therein all of which are incorporated herein by reference. In an alternate synthetic alkylation scheme (Alkylation Method-2), a "Generic Amine-2" of Formula XXII is reacted with a "Generic Bromide-2" of Formula XXIII in a method employing palliadium catalyzed carbon-nitrogen bond formation. Suitable procedures for this conversion are described in Wagaw and Buchwald, J. Org. Chem.(1996), 61, 7240-7241. Wolfe, Wagaw and Buchwald, J. Am. Chem. Soc. (1996), 118, 7215-7216, and Wolfe and Buchwald, Tetrahedron Letters (1997), 38(36), 6359-6362 and references cited therein all of which are incorporated herein by reference. The preferred "Generic Bromide-2" of Formula XXIII are generally aryl bromides, aryl Inflates, and heteroaryl bromides.

[0131] The "Generic Amine-1" and "Generic Amine-2" amines, hydroxylamines, and hydrazines, the "Generic Carbonyl Compound" aldehydes, ketones, hydrazones, and oximes, and "Generic Bromide-1" and "Generic Bromide-2" halides, tosylates, mesylates, triflates, and precursor alcohols required to prepare the "Generic Secondary Amine" compounds are available from commercial sources or can be prepared by one skilled in the art from published procedures. Commercial sources include but are not limited to Aldrich Chemical, TCI-America, Lancaster-Synthesis, Oakwood Products, Acros Organics, and Maybridge Chemical. Disclosed procedures for "Generic Amine" amines, hydroxylamines, and hydrazines include Sheradsky and Nov. J. Chem. Soc., Perkin Trans. 1 (1980), (12), 2781-6: Marcoux. Dove. and Buchwald, J. Am. Chem. Soc. (1997), 119, 1053-9; Sternbach and Jamison, Tetrahedron Lett. (1981), 22 (35), 3331-4; U. S. Patent No. 5306718; EP No. 314435; WO No. 9001874; WO No. 9002113: JP No. 05320117: WO No. 9738973; Swiss Patent No. CH 441366; U. S. Patents Nos. 3359316 and 3334017; and references cited therein which are incorporated herein by reference.

[0132] Synthetic Scheme 2 shows the preparation of the class of compounds corresponding to Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula 1-HPC("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") wherein A and Q are independently aryl and heteroaryl.

[0133] Derivatives of "Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols", "Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols", "Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols". "Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols", and "Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols", in which the hetero atom (-O-) is attached to an alkyl group removed from the amine by two or more carbons are readily prepared by anion chemistry using the method of Scheme 2. The anion of "Generic Secondary Amine" amines, hydroxylamines, and hydrazines of Formula XIII is readily formed by dissolving the specific amine, hydroxylamine, or hydrazine in an aprotic solvent, such as tetrahydrofuran, toluene, ether, dimethylformamide, and dimethylformamide, under anhydrous conditions. The solution is cooled to a temperature between -78 and 0°C, preferrably between -78 and -60°C, and the anion formed by the addition of at least one equivalent of a strong, aprotic, nonnucleophillic base, such as NaH or n-butyllithium under an inert atmosphere, for each acidic group present. Maintaining the temperature between -78 and 0°C, preferrably between -78 and -60°C, with suitable cooling, an appropriate alkyl halide, alkyl benzenesulfonate such as a alkyl tosylate, alkyl mesylate, alkyl triflate or similar alkylating reagent of the general structure:



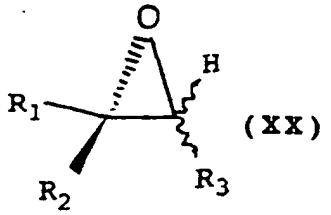
(XXX)

where M is a readily displaceable group such as chloride, bromide, iodide, tosylate, triflate, and mesylate and X is oxy. After allowing the reaction mixture to warm to room temperature, the reaction product is added to water, neutralized if necessary, and extracted with a water-immiscible solvent such as diethyl ether or methylene chloride. The combined aprotic solvent extract is washed with saturated brine, dried over drying agent such as anhydrous MgSO4 and concentrated *in vacuo* to yield crude Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). This material is purified, for example, by eluting through silica gel with a medium polar solvent such as ethyl acetate in a non-polar solvent such as hexanes to yield Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). Products are structurally confirmed by low and high resolution mass spectrometry and NMR.

[0134] Compounds of Formula (XXX), which can be used to prepare the "Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanol" compounds of Tables 3 and 4, are given in Table 2. Reagents 1a and 2a in Table 2 are prepared from the corresponding alcohols. (R)-Chiral alcohol precursors to 1a, 2a, and similiar alcohols that can be envisioned by one of inventive skill can be obtained from the corresponding racemic mixture of the R-enatiomer and S-enantiomer by separation procedures using preparative gas chromatography and high pressure liquid chromatography using chiral chromatographic columns. The tosylates of chiral alcohols and racemic mixtures are readily obtained by reacting the corresponding alcohol with tosyl chloride using procedures found in House's Modern Synthetic Reactions, Chapter 7, W. A. Benjamin, Inc., Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons. and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons, which are incorporated herein by reference.

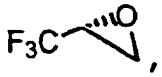
[0135] Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"). Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds can also be prepared using the method of Scheme 2 through the use of racemic (XXX) as described followed by preparative separation of the R-enantiomer from the S-enatiomer using chiral chromatographic procedures such as preparative gas chromatography and high pressure liquid chromatography using readily available chiral chromatographic columns and procedures.

[0136] A preferred procedure for Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds is the novel inventive Method A of Scheme 3. (R)-Chiral oxirane reagents useful in Method A are exemplified, but not limited to those in Table 1. Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds are prepared by reacting "Generic Secondary Amine" amines, hydroxylamines, and hydrazines of Formula XIII with (R)-chiral oxiranes of the type listed in Table 1 and represented by the general structure:



(XX)

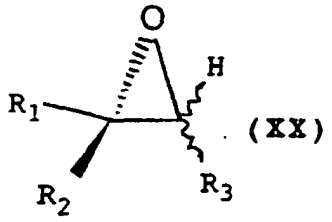
Oxiranes having a specific stereochemical arrangement of R_1, R_2 and R_3 can be prepared using chiral procedures such as those published in 1995 by Ramachandran, Gong, and Brown in the Journal of Organic Chemistry, Vol. 60. pages 41 to 46; cited references also detail alternate procedures to prepare chiral and achiral epoxides, which are incorporated herein by reference. For example, the specific preparation of *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane.



using a procedure adopted from H.C.Brown et al. (*J. Org. Chem.* **60**, 41-46, (1995)), is accomplished as described in **Example 4**. Many of the epoxides summarized in Table 1 can be prepared in the (R)-configuration using procedures analogous to that given above for *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane.

[0137] In some cases, achiral oxiranes of (XX) can be prepared from the corresponding alkenes by reaction of epoxidation reagents such as meta-chloroperbenzoic acid (MCPBA) and similar type reagents readily selectable by a person of skill-in-the-art with alkenes. Fieser and Fieser in Reagents for Organic Synthesis, John Wiley & Sons provides, along with cited references, numerous suitable epoxidation reagents and reaction conditions, which are incorporated herein by reference. These achiral oxiranes can be reacted in an identical manner to that described for (R)-chiral oxiranes with "Generic Secondary Amine" amines, hydroxylamines, and hydrazines of Formula XIII to afford racemic compounds structurally identical to those of Formula I-HP, Formula I-HPC, and Formula I-C but with the corresponding (S) chiral configuration present in an equivalent amount. Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds can be obtained by preparative chiral chromatography of said racemic mixtures to obtain the (R)-chiral configuration of Formula I-HP, Formula I-HPC, and Formula I-CP substantially free of the (S)-chiral configuration enantiomer. Alternatively, achiral oxiranes may be separated by chiral preparative chromatography into their respective (R)-Chiral and (S)-Chiral enantiomers and the (R)-Chiral enantiomer reacted to afford Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds.

Table 1. Structure of (R)-Chiral Oxirane Reagents.



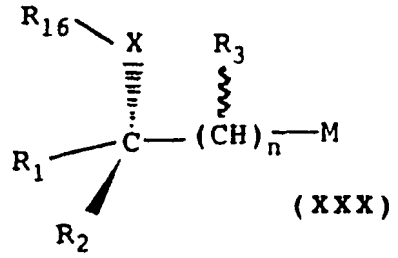
(XX)

Reagent Number	R_1	R_2	R_3
1	CF_3	H	H
2	CCl_3	H	H
3	CF_3	CH_3	H
4	CF_3CF_2	H	H
5	$CF_3CF_2CF_2$	H	H
6	$CF_3OCF_2CF_2$	H	H
7	CF_3CH_2	H	H
9	CF_3	H	CF_3
11	CF_3	C_6H_5	H
12	CCl_3	C_6H_5	H
13	CCl_3	Cyclopropyl	H
14	CCl_3	CH_3	H
15	CCl_3	$(CH_3)_2CH$	H
16	$CHCl_2$	H	H
18	CF_3	H	CH_3
27	CCl_3CH_2	H	H
28	CBr_3CH_2	H	H
29	$CHBr_2CH_2$	H	H
30	$CBrCl_2$	H	H
31	$CClF_2$	H	H
32	CCl_2F	H	H

Table 1. (continued) Structure of (R)-Chiral Oxirane Reagents.

Reagent Number	R_1	R_2	R_3
33	CCl_3CCl_2	H	H
43	FCH_2	H	H
56	$CBrF_2CClFCH_2$	H	H
57	$HCF_2CF_2OCH_2$	H	H

Table 2. Structure and Source of Alcohol and Glycol Reagents.

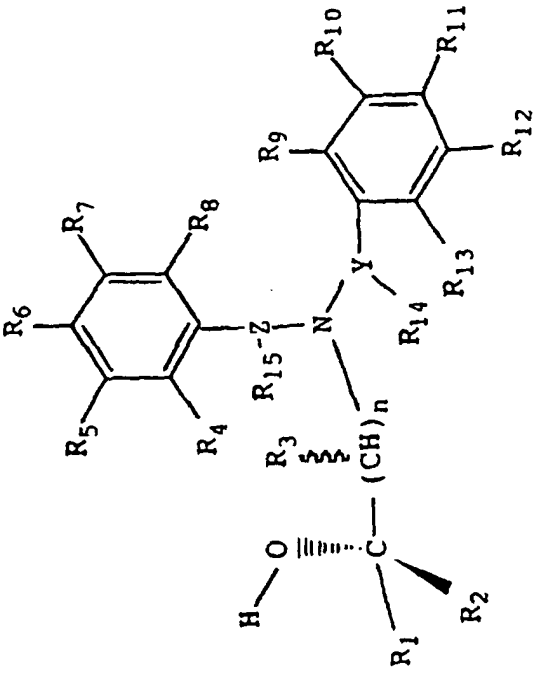


(XXX)

Reagent Number	R_1	n	M	R_2	R_3	X-R_{16}	Source of Reagent
1A	CF_3	3	OTs	H	H	OH	Chiral separation and then tosylation of alcohol from Justus Liebigs Ann. Chem. (1969), 720, 81-97.
2A	$CF_3CH_2CH_2$	3	OTs	H	H	OH	Chiral separation and then tosylation of alcohol from Z. Naturforsch., B: Chem. Sci. (1997), 52 (3). 413-418

Table 3. Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols

(Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).



Inhibitor Number Column1+Column 2	R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent									
IA	1N	3	H	H	H	C_6H_5O	H	H	OCF_2CF_2H	H
IA	2N	3	H	H	H	OCF_3	H	H	OCF_2CF_2H	H

Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
1A	3N	CF_3	3	H	H	F	H	H	F	OCF_2CF_2H	H
1A	4N	CF_3	3	H	H	H	F	H	H	OCF_2CF_2H	H
1A	5N	CF_3	3	H	H	H	C_6H_5O	H	H	OCF_3	H
1A	6N	CF_3	3	H	H	H	OCF_3	H	H	OCF_3	H
1A	7N	CF_3	3	H	H	H	H	phenyl	H	OCF_3	H
1A	8N	CF_3	3	H	H	H	phenyl	H	H	OCF_3	H
1A	9N	CF_3	3	H	H	H	H	H	H	OCF_3	H
1A	10N	CF_3	3	H	H	H	Br	H	H	OCF_3	H
1A	11N	CF_3	3	H	H	H	CF_3	F	H	CF_3	H
1A	12N	CF_3	3	H	H	H	CH_3	H	H	CF_3	H
1A	13N	CF_3	3	H	H	H	CF_3	H	H	CF_3	H
1A	14N	CF_3	3	H	H	H	CH_3	H	H	OCF_3	H

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Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
1A	15N	CF_3	3	H	H	H	F	F	H	OCF_3	H
1A	16N	CF_3	3	H	H	H	Br	H	H	CF_3	H
1A	17N	CF_3	3	H	H	H	CF_3	F	H	OCF_3	H
1A	18N	CF_3	3	H	H	H	F	H	H	OCF_3	H
1A	19N	CF_3	3	H	H	H	Cl	H	H	OCF_3	H
1A	20N	CF_3	3	H	H	H	F	H	H	CF_3	H
1A	21N	CF_3	3	H	H	H	F	F	H	CF_3	H
1A	22N	CF_3	3	H	H	H	Cl	H	H	CF_3	H
1A	23N	CF_3	3	H	H	H	F	H	H	phenoxy	H
1A	24N	CF_3	3	H	H	H	CF_3	Cl	H	CH_3	H
1A	25N	CF_3	3	H	H	H	CF_3	F	H	CH_3	H
1A	26N	CF_3	3	H	H	H	H	H	H	CF_3	H

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Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
1A	27N	CF_3	3	H	H	F	F	H	H	CF_3	H
1A	28N	CF_3	3	H	H	H	H	OCH_3	H	CF_3	H
1A	29N	CF_3	3	H	H	H	F	F	H	CH_3	H
1A	30N	CF_3	3	H	H	H	OCH_3	H	H	CH_3	H
1A	31N	CF_3	3	H	H	H	H	CH_3	H	H	H
1A	32N	CF_3	3	H	H	H	Cl	H	H	H	H
1A	33N	CF_3	3	H	H	H	F	H	H	F	H
1A	34N	CF_3	3	H	H	H	H	OCH_3	H	CH_3	H
1A	35N	CF_3	3	H	H	H	H	H	H	H	H
1A	36N	CF_3	3	H	H	H	H	CH_3	H	CH_3	H
1A	37N	CF_3	3	H	H	H	H	Cl	H	H	H
1A	38N	CF_3	3	H	H	H	F	H	H	3-CF_3-	H

Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
										phenoxy	
1A	39N	CF_3	3	H	H	H	F	H	H	4-CH_3O-phenoxy	H
1A	40N	CF_3	3	H	H	H	F	H	H	4-Cl-phenoxy	H
1A	41N	CF_3	3	H	H	H	F	H	H	H	H
1A	42N	CF_3	3	H	H	H	F	H	H	CH_3	H
1A	43N	CF_3	3	H	H	H	F	H	F	CH_3	H
1A	44N	CF_3	3	H	H	F	F	H	H	CH_3	H
1A	45N	CF_3	3	H	H	H	Cl	H	H	CH_3	H
1A	46N	CF_3	3	H	H	H	CH_3	H	H	CH_3	H
1A	48N	CF_3	3	H	H	H	H	CH_3	H	CF_3	H
1A	51N	CF_3	3	H	H	H	H	CH_3	H	F	H

Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column_2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
1A	52N	CF_3	3	H	H	H	CF_3	H	H	F	H
1A	53N	CF_3	3	H	H	H	CF_3	H	H	CH_3	H
1A	54N	CF_3	3	H	H	H	OCH_3	H	H	CF_3	H
1A	56N	CF_3	3	H	H	H	H	CH_3	H	CF_3	H
1A	57N	CF_3	3	H	H	H	C_6H_5O	H	H	H	OCF_3
1A	58N	CF_3	3	H	H	H	H	H	H	H	OCF_3
1A	59N	CF_3	3	H	H	H	OCF_3	H	H	H	OCF_3
1A	60N	CF_3	3	H	H	H	CF_3	F	H	H	CF_3
1A	61N	CF_3	3	H	H	H	H	OCH_3	H	H	CF_3
1A	62N	CF_3	3	H	H	H	CH_3	H	H	H	CF_3
1A	63N	CF_3	3	H	H	H	Cl	H	H	H	CF_3
1A	64N	CF_3	3	H	H	H	CF_3	H	H	H	OCF_3

Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
1A	65N	CF_3	3	H	H	H	F	H	H	H	OCF_3
1A	66N	CF_3	3	H	H	H	F	H	F	H	OCF_3
1A	67N	CF_3	3	H	H	H	Br	H	H	H	OCF_3
1A	68N	CF_3	3	H	H	H	Cl	H	H	H	OCF_3
1A	69N	CF_3	3	H	H	H	F	F	H	H	OCF_3
1A	70N	CF_3	3	H	H	H	F	H	H	H	phenyl
1A	71N	CF_3	3	H	H	H	CH_3	H	H	H	OCF_3
1A	72N	CF_3	3	H	H	H	F	F	H	H	CF_3
1A	73N	CF_3	3	H	H	H	Cl	H	H	H	CH_3
1A	74N	CF_3	3	H	H	H	OCH_3	H	H	H	CH_3
1A	75N	CF_3	3	H	H	H	F	H	H	H	CH_3
1A	76N	CF_3	3	H	H	F	F	H	H	H	OCF_3

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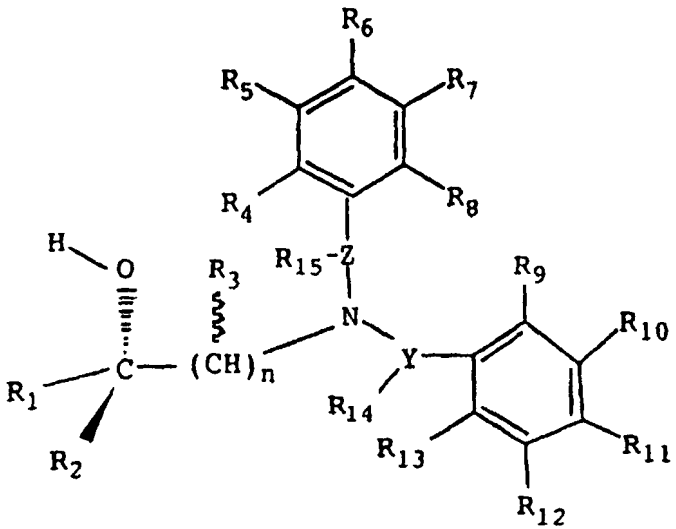
Table 3. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y is CH; R_8, R_9, R_{12}, R_{13}, and R_{14} are each H; Z is covalent bond and R_{15} is absent).

Inhibitor Number Column1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_7	R_{10}	R_{11}
Reagent	Reagent										
IA	78N	CF_3	3	H	H	H	H	OCH_3	H	H	CH_3
IA	79N	CF_3	3	H	H	H	H	CH_3	H	H	CH_3
IA	80N	CF_3	3	H	H	H	CH_3	H	H	H	CH_3
IA	82N	CF_3	3	H	H	H	F	F	H	H	CH_3
IA	83N	CF_3	3	H	H	H	F	H	F	H	CH_3
IA	84N	CF_3	3	H	H	F	F	H	H	H	CH_3
IA	85N	CF_3	3	H	H	F	CF_3	H	H	H	CH_3
IA	86N	CF_3	3	H	H	H	H	CH_3	H	H	CF_3
IA	88N	CF_3	3	H	H	H	CF_3	H	H	H	CH_3
IA	90N	CF_3	3	H	H	H	H	CF_3	H	H	CH_3
IA	92N	CF_3	3	H	H	H	CF_3	F	H	H	CH_3

Table 4. Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y and Z are each CH; R_8, R_9, R_{12}, R_{13}, R_{14} and R_{15} are each H).



Inhibitor Number Column 1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_9	R_{10}	R_{11}
Reagent	Reagent										
IA	IDB	CF_3	3	H	H	H	OCF_3	H	H	OCF_3	H

Table 4. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y and Z are each CH; R_8, R_9, R_{12}, R_{13}, R_{14} and R_{15} are each H).

Inhibitor Number Column 1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_9	R_{10}	R_{11}
Reagent	Reagent										
1A	2DB	CF_3	3	H	H	H	Cl	H	H	H	CF_3
1A	3DB	CF_3	3	H	H	H	Br	H	H	OCF_3	H
1A	4DB	CF_3	3	H	H	H	Cl	H	H	OCF_3	H
1A	5DB	CF_3	3	H	H	H	Cl	H	H	CF_3	H
1A	6DB	CF_3	3	H	H	H	H	Cl	H	CF_3	H
1A	7DB	CF_3	3	H	H	H	F	H	H	OCF_3	H
1A	8DB	CF_3	3	H	H	H	H	Cl	H	H	CF_3
1A	9DB	CF_3	3	H	H	H	F	H	H	H	CF_3
1A	10DB	CF_3	3	H	H	H	H	F	H	H	CF_3
1A	11DB	CF_3	3	H	H	F	H	H	H	H	CF_3
1A	12DB	CF_3	3	H	H	H	Cl	H	CF_3	H	H

Table 4. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols (Y and Z are each CH; R_8, R_9, R_{12}, R_{13}, R_{14} and R_{15} are each H).

Inhibitor Number Column 1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_9	R_{10}	R_{11}
Reagent	Reagent										
1A	13DB	CF_3	3	H	H	H	H	Cl	CF_3	H	H
1A	14DB	CF_3	3	H	H	Cl	H	H	CF_3	H	H
1A	15DB	CF_3	3	H	H	H	F	H	CH_3	H	H
1A	16DB	CF_3	3	H	H	H	H	F	H	H	CH_3
1A	17DB	CF_3	3	H	H	H	F	H	H	CH_3	H
1A	18DB	CF_3	3	H	H	F	H	H	CH_3	H	H
1A	19DB	CF_3	3	H	H	H	H	F	H	CH_3	H
1A	20DB	CF_3	3	H	H	F	H	H	H	H	CH_3
1A	21DB	CF_3	3	H	H	F	H	H	H	CF_3	H
1A	22DB	CF_3	3	H	H	Cl	H	H	H	CF_3	H
1A	23DB	CF_3	3	H	H	H	F	H	CF_3	H	H

Table 4. (continued) Structure of Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols

(Y and Z are each CH; R_8, R_9, R_{12}, R_{13}, R_{14} and R_{15} are each H).

Inhibitor Number Column 1+Column 2		R_1	n	R_2	R_3	R_4	R_5	R_6	R_9	R_{10}	R_{11}
Reagent	Reagent										
1A	24DB	CF_3	3	H	H	H	H	F	CF_3	H	H
1A	25DB	CF_3	3	H	H	H	F	H	H	CF_3	H
1A	26DB	CF_3	3	H	H	H	H	F	H	CF_3	H
1A	27DB	CF_3	3	H	H	H	OCF_3	H	H	H	OCF_3

[0138] A mixture of a "Generic Secondary Amine" amine, hydroxylamine, or hydrazine of Formula XIII and an excess of a halogenated oxirane of (R)-chiral configuration of Formula XX are stirred and heated to 40-90°C for 5 to 48 hours in a tightly capped or contained reaction vessel. More preferrably, a Lewis acid such as a transition metal-based salts (for example, ytterbium triflate, hafnium triflate, scandium triflate, neodynium inflate, gadolium triflate, and zirconium triflate) in methylene chloride, tetrahydrofuran, or, more preferrably, acetonitrile is added to speed up the reaction to a total time of 4 to 18 hours, improve yields, to permit the reaction temperature to be reduced to 15-65°C, and to use a smaller excess of halogenated oxirane. When a Lewis acid is used. the reaction should be carried out under inert, anhydrous conditions using a blanket of dry nitrogen or argon gas. After cooling to room temperature and testing the

reaction mixture for complete reaction by thin layer chromatography or high pressure liquid chromatography (hplc), the reaction product is added to water and extracted with a water immiscible solvent such as diethyl ether or methylene chloride. (Note: If the above analysis indicates that reaction is incomplete, heating should be resumed until complete with the optional addition of more of the oxirane). The combined aprotic solvent extract is washed with saturated brine, dried over drying agent such as anhydrous $MgSO_4$ and concentrated *in vacuo* to yield crude Formula 1-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds. This material is purified by eluting through silica gel with 5-40% of a medium polar solvent such as ethyl acetate in a non-polar solvent such as hexanes to yield Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds. Products are tested for purity by HPLC. If necessary, the Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds are purified by additional chromatography or recrystallization. Products are structurally confirmed by low and high resolution mass spectrometry and NMR. Examples of specific Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula 1-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds prepared are summarized in the Examples 1 through 44, and Example Tables 1 through 12.

[0139] Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds can further be prepared in an alternate manner to procedures disclosed above and in Schemes 1, 2, and 3. Schemes 9 and 10 detail such procedures to prepare aminopropanol compounds by initial formation of an halogenated, oxygen containing primary alkylamine XVL ("Generic Substituted Alkylamine"). Said halogenated, oxygen containing primary alkylamine XVL, formed in Scheme 9, is itself converted to secondary amines, VLX-H ("Heteroaryl Alkyl Amine) and VLX ("Phenyl Alkyl Amine"), using procedures disclosed above. Primary alkylamine XVL is first reacted with an aldehydic or ketonic carbonyl compound, XI-AH ("Heteroaryl Carbonyl") with azeotropic distillation to form imine, VL-H ("Heteroaryl Imine"). Said imine VL-H is then reduced with or without prior isolation by Reduction Methods 1, 2 or 3 as disclosed above and in Scheme 1 to yield secondary amine. VLX-H ("Heteroaryl Alkyl Amine). Said secondary amine VLX-H can be converted according to Scheme 10 to give Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols") and Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds. Using similar Schemes, VLX can be converted to Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds. Compounds in which one aromatic substituent is aryl and the other aromatic substitutent is heteroaryl can be readily prepared by reacting VLX-H with an aralkyl bromide or aryl bromide instead of using an heteroaralkyl bromide or heteroaryl bromide. Similarly, compounds in which one aromatic substituent is aryl and the other aromatic substituted is heteroaryl can be readily prepared by reacting VLX with an heteroaryl bromide or heteroaralkyl bromide instead of using an aryl bromide or an aralkyl bromide.

[0140] Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds can further be prepared in an alternate manner to procedures disclosed above and in Schemes 1, 2, 3, 9, and 10. Schemes 13, 14, and 15 detail alternate procedures to prepare (R)-Chiral Halogenated 1-Substitutedamino-2-propanols" compounds by initial formation of an halogenated, oxygen containing secondary alkylamines VLX and VLXX ("Phenyl Alkylamines") and VLXX-O ("Phenyl Oxy Alkylamines"). Said secondary alkylamines VLX and VLXX ("Phenyl Alkylamines") and VLXX-O ("Phenyl Oxy Alkylamines") can be converted according to Schemes 13, 14, and 15 to Formula 1-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with appropriate aromatic halides such as aryl bromides and heteroaryl bromides as desired.

[0141] Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formuta I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds can further be prepared in an alternate manner to procedures disclosed above and in Schemes 1, 2, 3, 9, 10, 13, 14, and 15. Another alternate procedure to prepare "(R)-Chiral Halogenated 1-Substitutedamino-2-propanols" compounds can be achieved

by reacting secondary amines of Formula XIIIA-H ("Secondary Heteroaryl Amines") and Formula XIII-A ("Secondary Phenyl Amines") with certain cyclic sulfates. Cyclic sulfates useful in the preparation of "(R)-Chiral Halogenated 1-Substitutedamino-2-propanols" compounds of Formulas I-HP, I-HPC, and I-CP have a halogenated or haloalkoxy carbon adjacent to the cyclic sulfate. Some cyclic sulfates useful for the preparation of "(R)-Chiral Halogenated 1-Substitutedamino-2-propanols" compounds of Formulas I-HP, I-HPC, and I-CP have been described by K. P. M. Vanhessche and K. B. Sharpless in Chem. Eur. J. 1997, Vol. 3, No. 4, pages 517-522 and references cited therein. (2R)-(+)-3,3,3-Trifluoro-1,2-propanediol can be prepared as described in the reference cited immediately above from 3,3,3-trifluoropropene followed by separation from the predominating (2S)-(-)-3,3,3-trifluoro-1,2-propanediol. Alternatively, (2R)-(+)-3,3,3-Trifluoro-1,2-propanediol can be prepared by hydrolysis of (2R)-(+)-3,3,3-Trifluoro-2,3-epxoypropane analogous to the procedure described by described by McBee and Burton in J. Am. Chem. Soc.. 1952, Vol. 74, page 3022. (2R)-(+)-3,3,3-Trifluoro-1,2-propanediol is converted by reaction with a slight excess of sulfuryl chloride in the presence of 2.5 molar equivalents of imidazole, methylene chloride solvent, and at a temperature of -20 °C to give the desired (4R)-(+)-4-trifluoromethyl-2,2-dioxo-1,3,2-dioxathiolane. Reaction of other (R)-Chiral haloalkyl or haloalkoxyalkyl substituted 1,2-ethanediols can afford the corresponding (4R)-substituted-2,2-dioxo-1,3,2-dioxathiolanes. Reaction of (4R)-(+)-4-trifluoromethyl-2,2-1,3,2-dioxathiolane or another (4R)-substituted-2,2-dioxo-1,3,2-dioxathiolane with a secondary amine of Formula XIIIA-H ("Secondary Heteroaryl Amines") and Formula XIII-A ("Secondary Phenyl Amines") in an anhydrous polar, non-protic solvent such as tetrahydrofuran or acetonitrile at 25-60 °C until the reaction is complete can afford the mono-sulfate ester of a compound of Formulas I-HP, I-HPC, and I-CP. Removal of the solvent followed by addition of diethyl ether and excess 20% aqueous sulfuric acid can lead to a precipitant of the crude mono-sulfate ester of a compound of Formulas I-HP, I-HPC, and I-CP. This precipitant can be filtered, the solid can be washed with ether, it can be resuspended in aqueous 20% sulfuric acid, and can be heated to 80-95 °C to give an aqueous solution of the sulfate salt of crude a compound of Formulas I-HP, I-HPC, and I-CP. Neutralization of the aqueous solution, extraction with a water immiscible solvent such as diethyl ether or methylene chloride, drying the organic solvent over anhydrous magnesium sulfate, and removal of solvent can afford a compound of Formulas I-HP, I-HPC, and I-CP. Compounds of Formulas I-HP, I-HPC, and I-CP can be purified as described previously. By using a wide variety of (R)-Chiral diols, secondary amines of Formula XIIIA-H ("Secondary Heteroaryl Amines") and Formula XIII-A ("Secondary Phenyl Amines"), and reaction conditions described herein, a large variety of compounds of Formulas I-HP, I-HPC, and I-CP may be preparable.

[0142] A particularly useful procedures to prepare Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"). Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula 1-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds in which the heteroaryl group is directly bonded is disclosed in Schemes 11 and 12. An halogenated, hydroxy containing primary alkylamine XVL ("Generic Substituted Alkylamine") formed according to Scheme 9 is itself converted by reaction with LXXI-AH ("Heteroaryl Halide") to afford secondary amine VLXX-H ("Heteroaryl Secondary Amine) using procedures disclosed in Scheme 11 and above. VLXX-H is converted to Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by alkylation chemistry with an aralkyl bromide or aralkyloxyalkyl bromide using either of two procedures disclosed in Scheme 12. Isolation and purification is effected as disclosed previously.

[0143] Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Haloaenated 1-Substitutedamino-2-Propanols") compounds can themselves serve as intermediates for conversion to additional compounds of this invention. Compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC and others useful as intermediates include those in which the R_7 position substituent in Formulas I-H, I-HP, I-C, I-CP, and I-HPC is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxycarbonyl or other alkoxy carbonyl groups, cyano group, or acyl group. Other preferred compounds of Formulas I-H, 1-HP, I-C, I-CP, I-HPC useful as intermediates include those in which the R_{10} position substituent is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxy carbonyl or other alkoxy carbonyl groups, cyano group, or acyl groups. Other compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC useful as intermediates include those in which one or more of R_6 , R_7 , R_{11} , and R_{12} substituents in Formula VII is a bromo group, hydroxyl group, sulfhydryl group, bromomethyl or other bromoalkyl groups, nitro group, amino group, methoxy carbonyl or other alkoxy carbonyl groups, cyano group, or acyl groups.

[0144] A 3-bromo substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Bromophenyl (R)-Chiral Halogenated

1-Substitutedamino-2-Propanols") compounds can be reacted with a phenol to afford, as described in **Examples,** 3-phenoxy compounds of the present invention of Formula I-CP ("Polycyclic 3-Phenoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0145] A 3-bromo substituent at the R_7 position in Formula I-HP and I-HPC ("Polycyclic 3-Bromophenyl amd 3-Bromoheteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") can, as shown in Scheme 4, be reacted with a phenol to afford, as described in **Examples**, additional compounds of Formula I-HP and I-HPC ("Polycyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl, 3-Heteroaryloxyheteroaryl, 3-Aryloxyheteroaryl , 3-Arylthioaryl, 3-Heteroarylthioaryl, 3-Heteroarylthioheteroaryl, and 3-Arylthioheteroaryl Aryl amd Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0146] A 3-bromo substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Bromophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") can be reacted, as shown in Scheme 7, with an aryl borinate or an aryl tin to afford, as described in **Examples,** additional compounds of Formula I-CP ("Polycyclic 3-Arylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0147] Scheme 8 discloses the conversion of a 3-bromo substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Bromophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with a primary or secondary amine to afford, as described in **Examples,** additional compounds of Formula I-CP ("Polycyclic 3-R_{22}aminophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0148] Conversion of a 3-bromo substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Bromophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an aryl borinate can afford, as described in **Examples,** additional compounds of Formula I-CP ("Polycyclic 3-Arylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0149] Conversion of a 3-bromo substituent at the R_{10} position in Formula 1-CP ("Polycyclic 3-Bromophenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with a heteroaryl dibutyl tin compound can afford, as described in **Examples,** additional compounds of the present invention of Formula I-CP ("Polycyclic 3-Heteroarylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0150] Conversion of a 3-bromomethyl substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Bromomethylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") by reaction with an aryl borinate can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-Arylmethylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0151] Scheme 5 discloses the conversion of a 3-hydroxyl substituent at the R_7 position in Formula I-HP and I-HPC ("Polycyclic 3-Hydroxyphenyl amd 3-Hydroxyheteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") by reaction with an aryl bromide or heteroaryl bromide to afford, as described in **Examples,** additional compounds of Formula I-HP and I-HPC ("Polycyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl, 3-Heteroaryloxyheteroaryl, and 3-Aryloxyheteroaryl Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0152] Conversion of a 3-hydroxyl substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Hyroxyphenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an aryl bromide can afford, as described in **Examples,** additional compounds of Formula I-CP ("Polycyclic 3-Phenoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0153] Conversion of a 3-hydroxyl substituent at the R_7 position in Formula I-HP and I-HPC ("Polycyclic 3-Hydroxyphenyl amd 3-Hydroxyheteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an aralkyl bromide or heteroaralkyl bromide can afford, as described above for Scheme 5 and in **Examples**, additional compounds of Formula I-HP and I-HPC ("Polycyclic 3-Aralkyloxyaryl, 3-Heteroaralkyloxyaryl, 3-Heteroaralkyloxyheteroaryl, and 3-Aralkyloxyheteroaryl Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0154] Conversion of a 3-hydroxyl substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Hyroxyphenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an aralkyl bromide can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-Aralkyloxyaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0155] Conversion of a 3-hydroxyl substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Hyroxyphenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an R_{17}-bromide can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3- R_{17}-oxyaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0156] Conversion of a 3-thio substituent at the R_7 position in Formula I-CP ("Polycyclic 3-thiophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an R_{17}-bromide can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3- R_{17}thiaaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). "Polycyclic 3- R_{17}thiaaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols" can be oxidized to sulfonyl compounds of Formula I-CP ("Polycyclic 3- R_{17}sulfonylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0157] Conversion of a 3-nitro substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Nitrophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by hydrogenation can afford, as described in **Examples**. additional compounds of Formula I-CP ("Polycyclic 3-Aminophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). "Polycyclic 3-Aminophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols" can be acylated to acyl amide compounds of Formula I-CP ("Polycyclic 3-R_{17}-C(O)amidophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0158] Conversion of a 3-amino substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Aminophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with carbonyl compounds can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-(Saturated Nitrogen Heterocycl-1yl)aryl (R)-Chiral Halogenated I-Substitutedamino-2-Propanols" and ("Polycyclic 3-(Unsaturated Nitrogen Heterocycl-1yl)aryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0159] Conversion of a 3-methoxycarbonyl substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with amination reagents can afford, as described in **Examples**. additional compounds of Formula I-CP ("Polycyclic 3-Carboxamidophenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0160] Conversion of a 3-cyano substituent at the R_7 position in Formula I-CP ("Polycyclic 3-Cyanophenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with organometallic reagents can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-Acylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). Said "Polycyclic 3-Acylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols" can be reduced to hydroxyl compounds of Formula I-CP ("Polycyclic 3-hydroxysubstitutedmethylphenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0161] Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with amination reagents can afford, as described in **Examples**, additional compounds of Formula I-CP "Polycyclic 3-Carboxamdophenyl (R) -Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0162] Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an organometallic reagent can afford, as described in **Examples**, additional compounds of Formula I-CP "Polycyclic 3-(bis- R_{20}-hydroxymethyl)aryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0163] Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with lithium aluminum hydride can afford, as described in **Examples**. additional compounds of Formula I-CP ("Polycyclic 3-Hydroxymethylphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0164] Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction with an alkylation reagent can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-(bis- R_{21}-hydroxymethyl)phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0165] Conversion of a 3-methoxycarbonyl substituent at the R_{10} position in Formula I-CP ("Polycyclic 3-Carbomethoxyphenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") compounds by reaction intially with an amidation reagent and then an R_{20}-organometallic reagent can afford, as described in **Examples**, additional compounds of Formula I-CP ("Polycyclic 3-(R_{20}-carbonyl)phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols").

[0166] Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"). Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") and other compounds posssessing hydroxyl, thiol, and amine functional groups can be converted to a wide variety derivatives. The hydroxyl group, wherein R_{16} is a hydrogen and X is oxy, of compounds of Formulas I-H, I-HP, I-HPC, I-C, and I-CP can be readily converted to esters of carboxylic, sulfonic, carbamic, phosphonic, and phosphoric acids. Acylation to form a carboxylic acid ester is readily effected using a suitable acylating reagent such as an aliphatic acid anhydride or acid chloride. The corresponding aryl and heteroaryl acid anhydrides and acid chlorides can also be used. Such reactions are generally carried out using an amine catalyst such as pyridine in an inert solvent. In like manner, compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one hydroxyl group present in the form of an alcohol or phenol can be acylated to its corresponding esters. Similarly, carbamic acid esters (urethans) can be obtained by reacting any hydroxyl group with isocyanates and carbamoyl chlorides. Sulfonate, phosphonate, and phosphate esters can be prepared using the corresponding acid chloride and similar reagents- Compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one thiol group present can be converted to the corresponding thioesters derivatives analogous to those of alcohols and phenols using the same reagents and com-

parable reaction conditions. Compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one primary or secondary amine group present can be converted to the corresponding amide derivatives. Amides of carboxylic acids can be prepared using the appropriate acid chloride or anhydrides with reaction conditions analogous to those used with alcohols and phenols. Ureas of the corresponding primary or secondary amine can be prepared using isocyanates directly and carbamoyl chlorides in the presence of an acid scavenger such as triethylamine or pyridine. Sulfonamides can be prepared from the corresponding sulfonyl chloride in the presence of aqueous sodium hydroxide. Suitable procedures and methods for preparing these derivatives can be found in House's Modem Synthetic Reactions, W. A. Benjamin, Inc., Shriner, Fuson, and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons. Reagents of a wide variety that can be used to derivatize hydroxyl, thiol, and amines of compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP are available from commerical sources or the references cited above, which are incorporated herein by reference.

[0167] Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") and other compounds posssessing hydroxyl, thiol, and amine functional groups can be alkylated to a wide variety derivatives. The hydroxyl group, wherein R_{16} is a hydrogen and X is oxy, of compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP can be readily converted to ethers. Alkylation to form an ether is readily effected using a suitable alkylating reagent such as an alkyl bromide, alkyl iodide or alkyl sulfonate. The corresponding aralkyl, heteroaralkyl, alkoxyalkyl, aralkyloxyalkyl, and heteroaralkyloxyalkyl bromides, iodides, and sulfonates can also be used. Such reactions are generally carried out using an alkoxide forming reagent such as sodium hydride, potassium t-butoxide, sodium amide, lithium amide, and n-butyl lithium using an inert polar solvent such as DMF, DMSO, THF, and similar, comparable solvents. In like manner, compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one hydroxyl group present in the form of an alcohol or phenol can be alkylated to their corresponding ethers. Compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one thiol group present can be converted to the corresponding thioether derivatives analogous to those of alcohols and phenols using the same reagents and comparable reaction conditions. Compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP that have at least one primary, secondary or tertiary amine group present can be converted to the corresponding quaternary ammonium derivatives. Quaternary ammonium derivatives can be prepared using the appropriate bromides, iodides, and sulfonates analogous to those used with alcohols and phenols. Conditions involve reaction of the amine by warming it with the alkylating reagent with a stoichiometric amount of the amine (i.e., one equivalent with a tertiary amine, two with a secondary, and three with a primary). With primary and secondary amines, two and one equivalents, respectively, of an acid scavenger are used concurrently. Tertiary amines can be preparedfrom the corresponding primary or secondary amine by reductive alkylation with aldehydes and ketones using reduction methods 1, 2, or 3 as shown in Scheme 1. Suitable procedures and methods for preparing these derivatives can be found in House's Modem Synthetic Reactions, W. A. Benjamin, Inc., Shriner. Fuson. and Curtin in The Systematic Indentification of Organic Compounds, 5th Edition, John Wiley & Sons, and Fieser and Fieser in Reagents for Organic Synthesis, Volume 1, John Wiley & Sons. Perfluoroalkyl derivatives can be prepared as described by DesMarteau in J. Chem. Soc. Chem. Commun. 2241 (1998). Reagents of a wide variety that can be used to derivatize hydroxyl, thiol, and amines of compounds of Formulas I-H, I-HP, I-C, I-CP, I-HPC, Cyclo I-H, Cyclo I-C, and Cyclo I-CP are available from commerical sources or the references cited above, which are incorporated herein by reference.

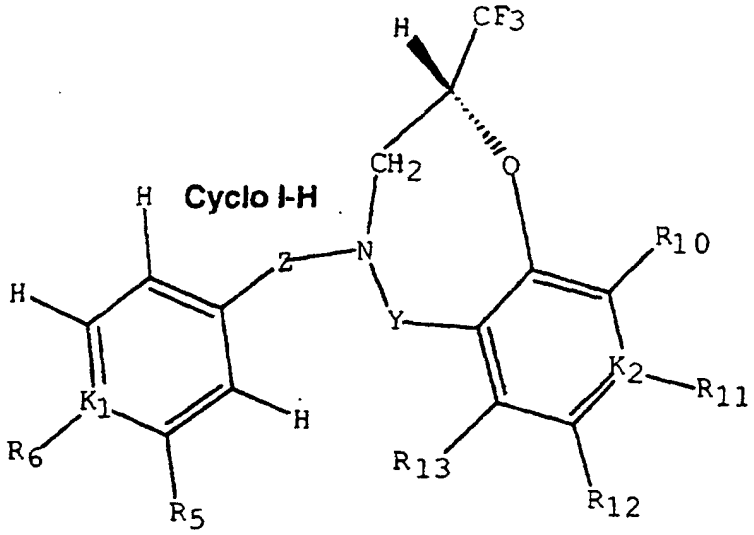
[0168] Formula I-H ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-alkanols"), Formula I-HP ("Generic Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated I-Substitutedamino-2-propanols"), Formula I-HPC ("Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols"), Formula I-C ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols"), and Formula I-CP ("Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols") and certain other compounds of this invention can be convened, according to Scheme 6, to the corresponding cyclic derivatives represented by "Tricyclic *tertiary*-oxyalkylamines" and exemplified by Formulas Cyclo I-H ("Polycyclic Aryl and Heteroaryl (R)-Chiral Halogenated (N+1) -Cycloazaalkoxy"), Cyclo I-C ("Polycyclic Aryl Phenyl (R)-Chiral Halogenated (N+1)-Cycloazaalkoxy") and Cyclo I-CP ("Polycyclic Phenyl Phenyl (R)-Chiral Halogenated Cycloazaalkoxy"). The hydroxyl group, wherein R_{16} is a hydrogen and X is oxy, of compounds of Formulas I-H, I-HP, I-C, I-CP, and I-HPC can be cyclized to corresponding cyclic ethers. Compounds suitable for cyclization will normally have at least one leaving group within 5 to 10 continuous atoms of the hydroxyl group wherein R_{16} is a hydrogen and X is oxy. Most preferrably the leaving group will be within 5 to 7 atoms of the hydroxyl group so as to form a 6 to 8 membered ring heteroatom containing ring. When the leaving group is part of an aromatic ring system, the leaving group will be preferrably in an ortho position. Suitable leaving groups generally include halides, sulfates, sulfonates, trisubsituted amino, disubstituted sulfonium, diazonium, and like, and.

in the case of aromatic systems, also includes nitro, alkoxy, aryloxy, heteroaryloxy, and alkylthio.

[0169] The cyclization reaction to form "Tricyclic *tertiary*-oxyalkylamines" of Formulas Cyclo I-H, Cyclo I-C and Cyclo I-CP can be accomplished by aromatic and aliphatic nucleophilic substitution reactions such as those disclosed in March's Advanced Organic Chemistry, 4th Edition, John Wiley & Sons, especially at pages 293-412 and 649-658 and the references cited therein, which are incorporated herein by reference. Hydroxyl containing suitably substituted compounds can be converted to a cyclic analog by heating a suitably substituted compound under anhydrous conditions in a suitable solvent, such as dimethylformamide, dimethylsulfoxide, N-methylpyrrolidone, tetraglyme, or hexamethylphosphoramide, in the presence of a suitable base such as potassium carbonate, cesium carbonate, sodium hydroxide, potassium *tertiary*-butoxide, or lithium diisopropylamide. Alternately, sodium amide in anhydrous ammonia solvent can be used. Temperatures in the range of -20 °C to 200 °C can be used for time periods of 30 minutes to more than 24 hours. The preferred temperature can be selected by standard synthetic chemical technique balancing maximum yield, maximum purity, cost, ease of isolation and operation, and time required. Isolation of the "Tricyclic *tertiary*-oxyalkylamines" can be effected as described above for other tertiary-oxyalkylamines. Representative "Tricyclic *tertiary*-oxyalkylamines" prepared using the methodology described above are included in Table 5.

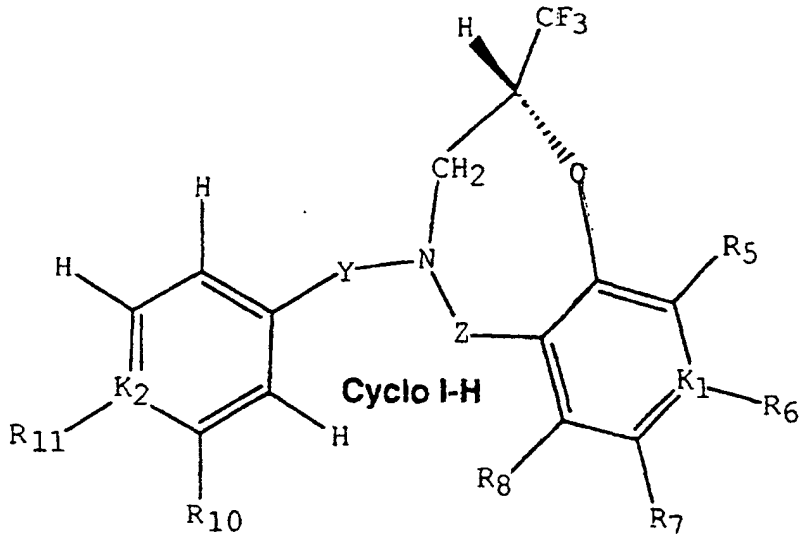
[0170] The following examples are provided to illustrate the present invention and are not intended to limit the scope thereof. Those skilled in the art will readily understand that known variations of the conditions and processes of the following preparative procedures can be used to prepare these compounds.

Table 5. Structure of Substituted Tricyclic*tertiary*-2-oxyalkylamines.



Y	Z	R_5	K_1-R_6	R_{10}	K_2-R_{11}	R_{12}	R_{13}
CH_2	-	4-chloro-3-ethylphenoxy	C-H	H	C- CF_3	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	H	C- CF_3	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	H	C- H	CF_3	H
CH_2	-	4-chloro-3-ethylphenoxy	N	H	C- H	CF_3	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	H	N	CF_3	H
-	-	4-chloro-3-ethylphenoxy	C-H	H	C- CF_3	H	H
-	-	4-chloro-3-ethylphenoxy	N	H	C- CF_3	H	H
-	-	4-chloro-3-ethylphenoxy	C-H	H	C- H	CF_3	H
-	-	4-chloro-3-ethylphenoxy	N	H	C- H	CF_3	H
-	-	4-chloro-3-ethylphenoxy	C-H	H	N	CF_3	H

Table 5. (cont.) Structure of Substituted Tricyclic *tertiary*-2-oxyalkylamines.

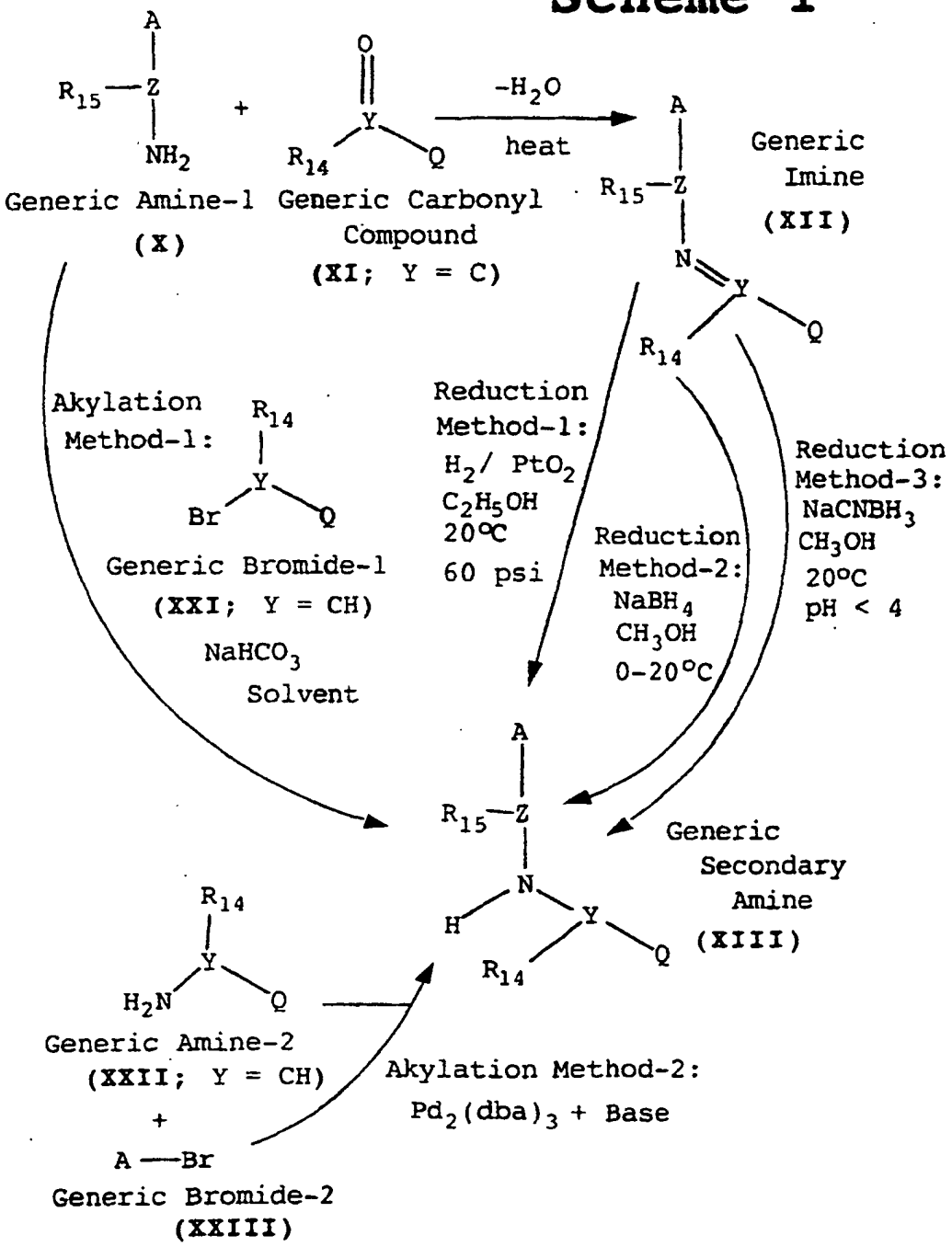


Y	Z	R_5	K_1-R_6	R_{10}	K_2-R_{11}	R_7	R_8
CH_2	-	4-chloro-3-ethylphenoxy	C-H	OCF_2CF_2H	C-H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	OCF_2CF_2H	C-H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	OCF_2CF_2H	N	H	H
CH_2	-	phenoxy	C-H	OCF_2CF_2H	C-H	H	H
CH_2	-	phenoxy	N	OCF_2CF_2H	C-H	H	H
CH_2	-	phenoxy	C-H	OCF_2CF_2H	N	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	CF_2CF_3	C-H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	CF_2CF_3	C-H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	CF_2CF_3	N	H	H
CH_2	-	phenoxy	C-H	CF_2CF_3	C-H	H	H
CH_2	-	phenoxy	N	CF_2CF_3	C-H	H	H
CH_2	-	phenoxy	C-H	CF_2CF_3	N	H	H

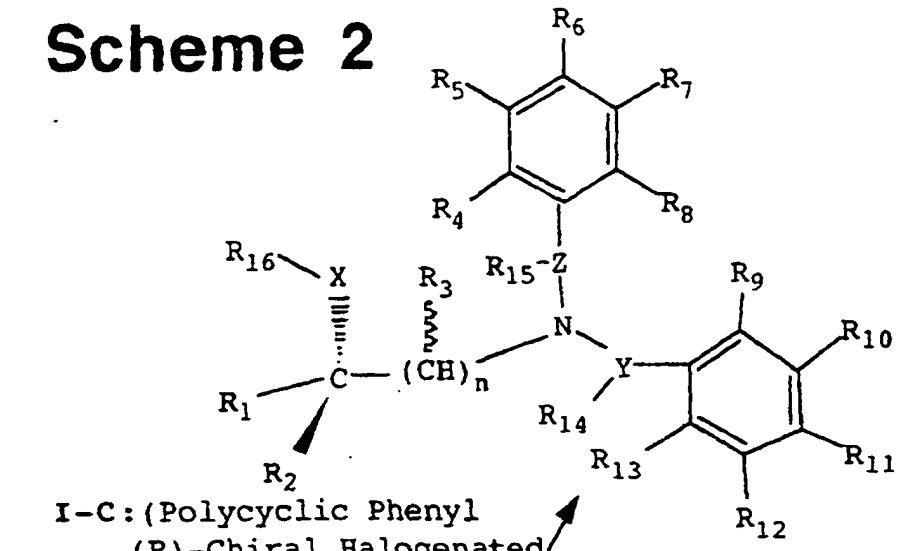
Table 5. (cont.) Structure of Substituted Tricyclic *tertiary*-2-oxyalkylamines.

Y	Z	R_5	K_1-R_6	R_{10}	K_2-R_{11}	R_7	R_8
CH_2	-	4-chloro-3-ethylphenoxy	C-H	CF_3	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	CF_3	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	CF_3	N	H	H
CH_2	-	phenoxy	C-H	CF_3	C- H	H	H
CH_2	-	phenoxy	N	CF_3	C- H	H	H
CH_2	-	phenoxy	C-H	CF_3	N	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	OCF_2CF_2H	C- H	H	F
CH_2	-	4-chloro-3-ethylphenoxy	N	OCF_2CF_2H	C- H	H	F
CH_2	-	4-chloro-3-ethylphenoxy	C-H	OCF_2CF_2H	N	H	F
CH_2	-	4-chloro-3-ethylphenoxy	C-H	2-furyl	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	2-furyl	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	2-furyl	N	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	SCF_3	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	N	SCF_3	C- H	H	H
CH_2	-	4-chloro-3-ethylphenoxy	C-H	SCF_3	N	H	H

Scheme 1


Generic Amine-1
(X)
Generic Carbonyl Compound
(XI; Y = C)
-H2O
heat
Generic Imine
(XII)
Akylation Method-1:
Generic Bromide-1
(XXI; Y = CH)
NaHCO3
Solvent
Reduction Method-1:
H2/ PtO2
C2H5OH
20°C
60 psi
Reduction Method-2:
NaBH4
CH3OH
0-20°C
Reduction Method-3:
NaCNBH3
CH3OH
20°C
pH < 4
Generic Secondary Amine
(XIII)
Generic Amine-2
(XXII; Y = CH)
+
A—Br
Generic Bromide-2
(XXIII)
Akylation Method-2:
Pd2(dba)3 + Base

Scheme 2



I-C: (Polycyclic Phenyl (R)-Chiral Halogenated 1-Substitutedamino-(n+1)-Alkanols)

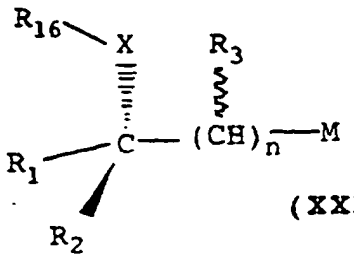
Method B:

Step 1:

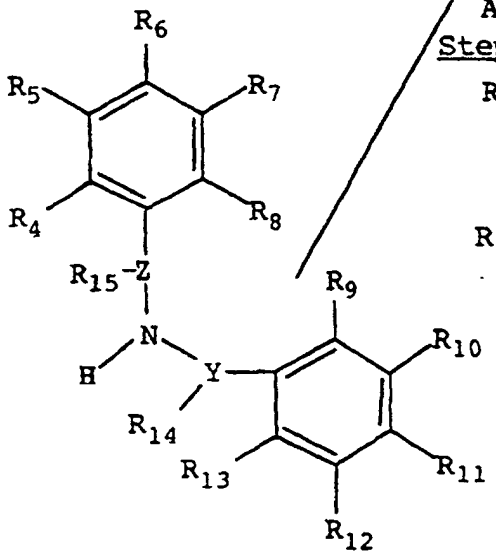
NaH or n-BuLi

Aprotic Solvent, -78 °C

Step 2:



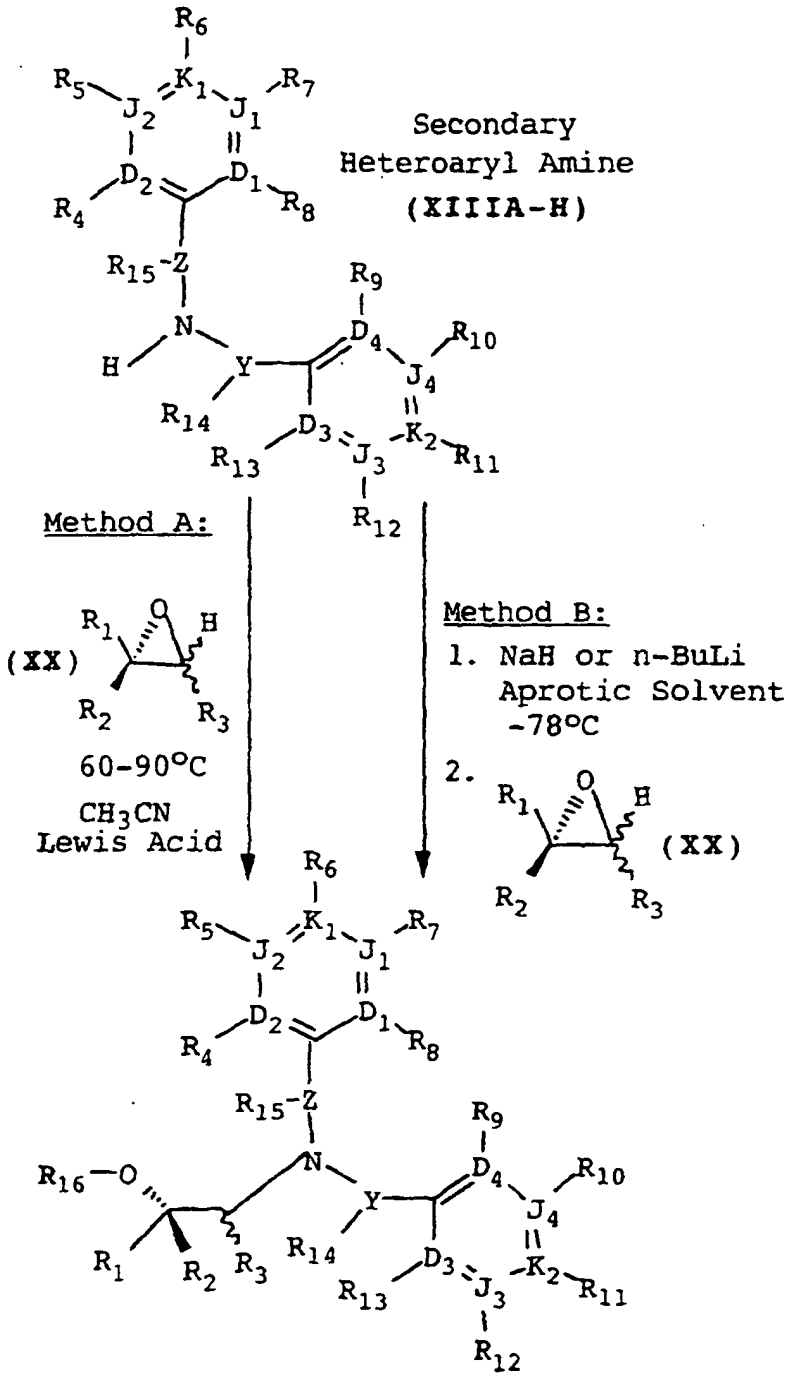
(XXX)



Secondary Phenyl Amine

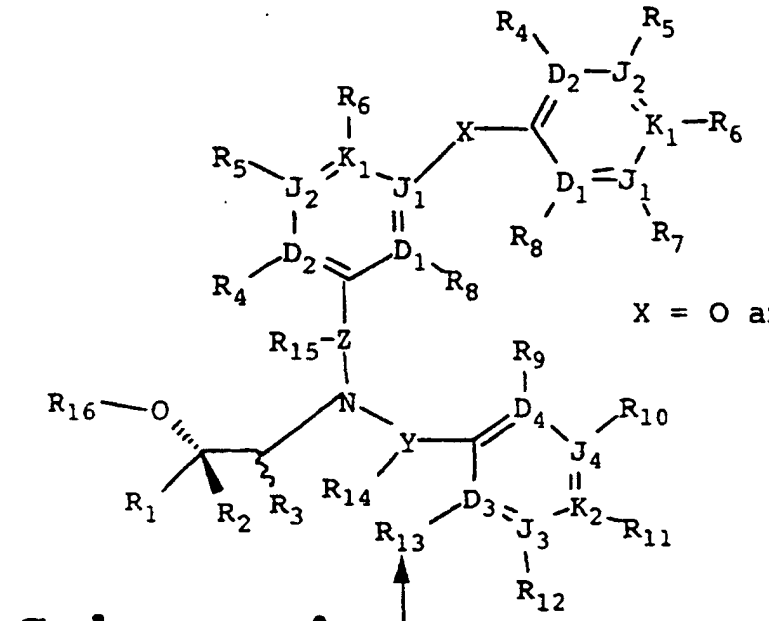
(XIIIA)

Scheme 3



I-HP/I-HPC: (Generic Polycyclic Aryl and Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols; R_{16} = H)

I-HP/I-HPC: (Generic Polycyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl, 3-Heteroaryloxyheteroaryl, 3-Aryloxyheteroaryl, 3-Arylthioaryl, 3-Heteroarylthioaryl, 3-Heteroarylthioheteroaryl, 3-Arylthioheteroaryl Aryl and Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)



X = O and S

Scheme 4

$Cu_2(triflate)_2 \cdot Benzene$

2 equivalents of Aryl-OH, Aryl-SH, Heteroaryl-OH, or Heteroaryl-SH

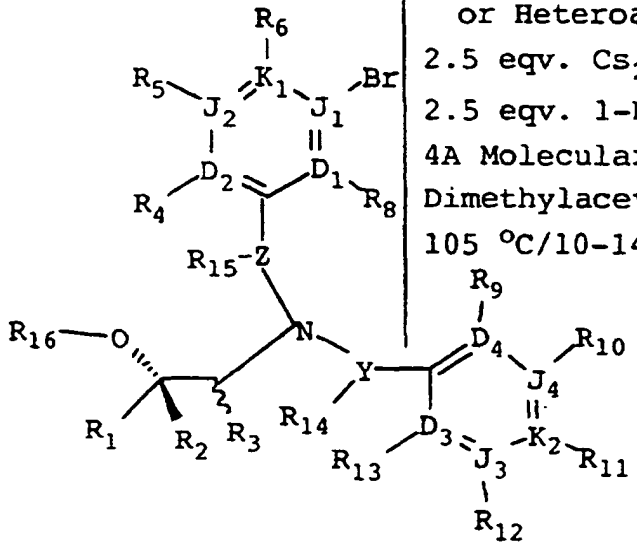
2.5 eqv. Cs_2CO_3

2.5 eqv. 1-Naphthoic Acid

4A Molecular Sieves

Dimethylacetamide/toluene

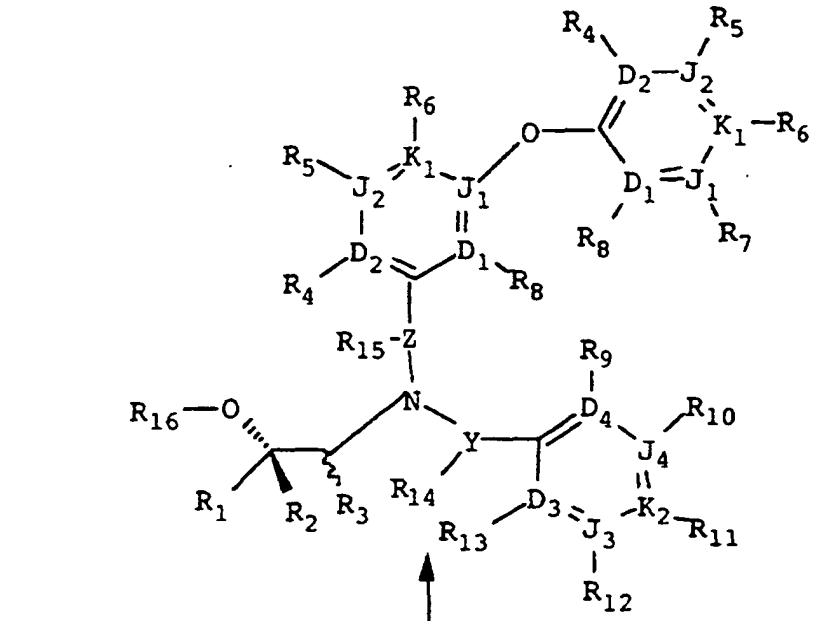
105 °C/10-14 Days



I-HP/I-HPC: (Generic Polycyclic 3-Bromo Aryl and Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

Scheme 5

I-HP/I-HPC: (Generic Polycyclic 3-Aryloxyaryl, 3-Heteroaryloxyaryl3-Aryloxyheteroaryl or 3-Heteroaryloxyheteroaryl Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)



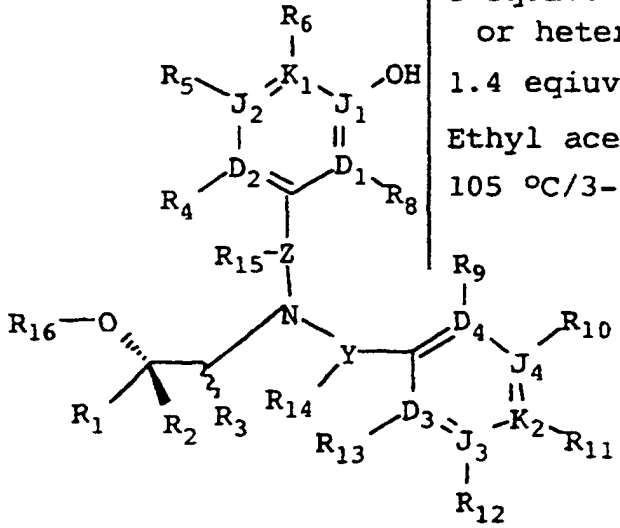
$Cu_2(triflate)_2 \cdot Benzene$

1 equiv. of aryl bromide or heteroaryl bromide

1.4 eqiuv. Cs_2CO_3

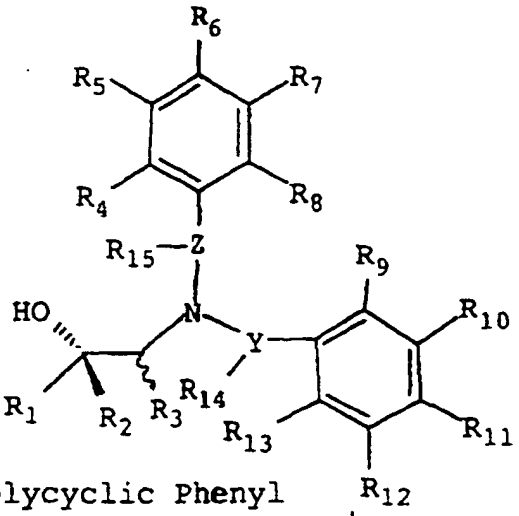
Ethyl acetate/toluene

105 °C/3-10 Days



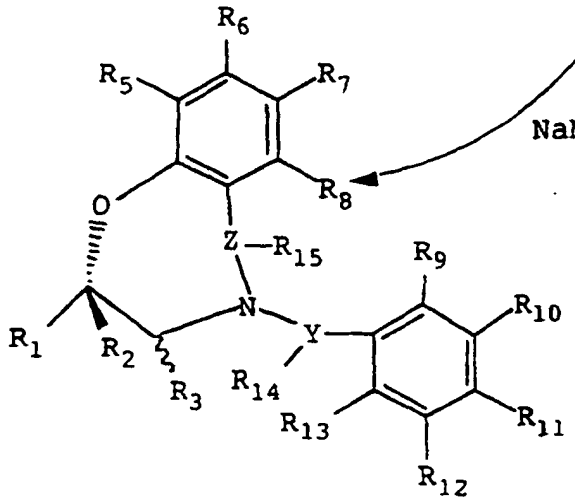
I-HP/I-HPC: (Generic Polycyclic 3-Hydroxy Aryl and Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

Scheme 6



I-CP: (Generic Polycyclic Phenyl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

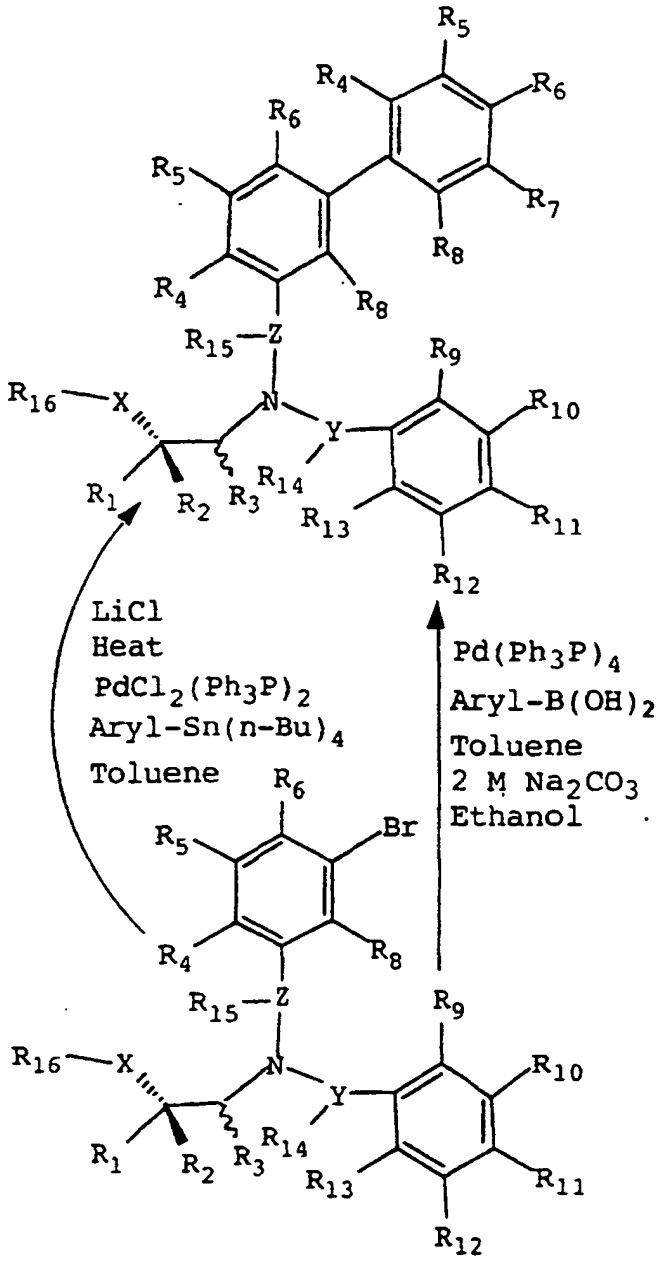
LDA/DMF
or
$NaNH_2/NH_3$



Cyclo I-CP: (Polycyclic Phenyl Phenyl (R)-Chiral Halogenated Cycloazaalkoxy)

Scheme 7

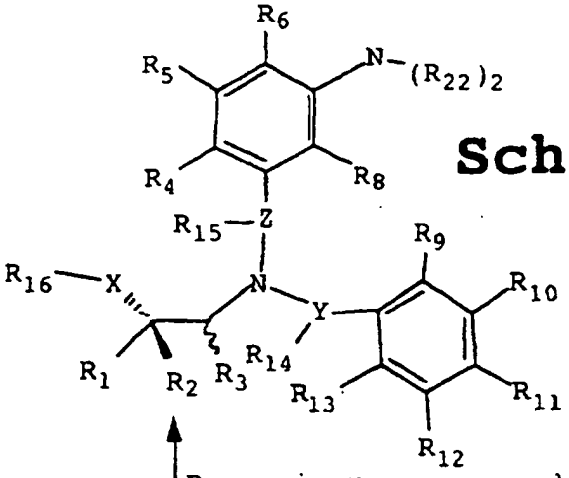
I-CP:(Polycyclic 3-Arylphenyl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)



I-CP:(Polycyclic 3-Bromophenyl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

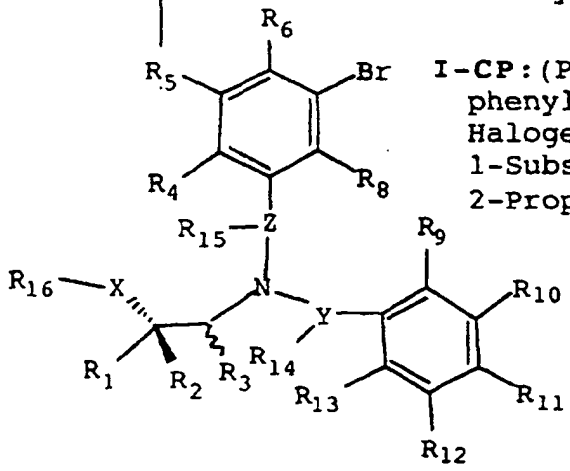
NOTE: Use of Heteroaryl-$B(OH)_2$ will give the heteroarylmethyl analog of **I-CP**.

I-CP:(Polycyclic 3-R_{22}-aminophenyl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)



Scheme 8

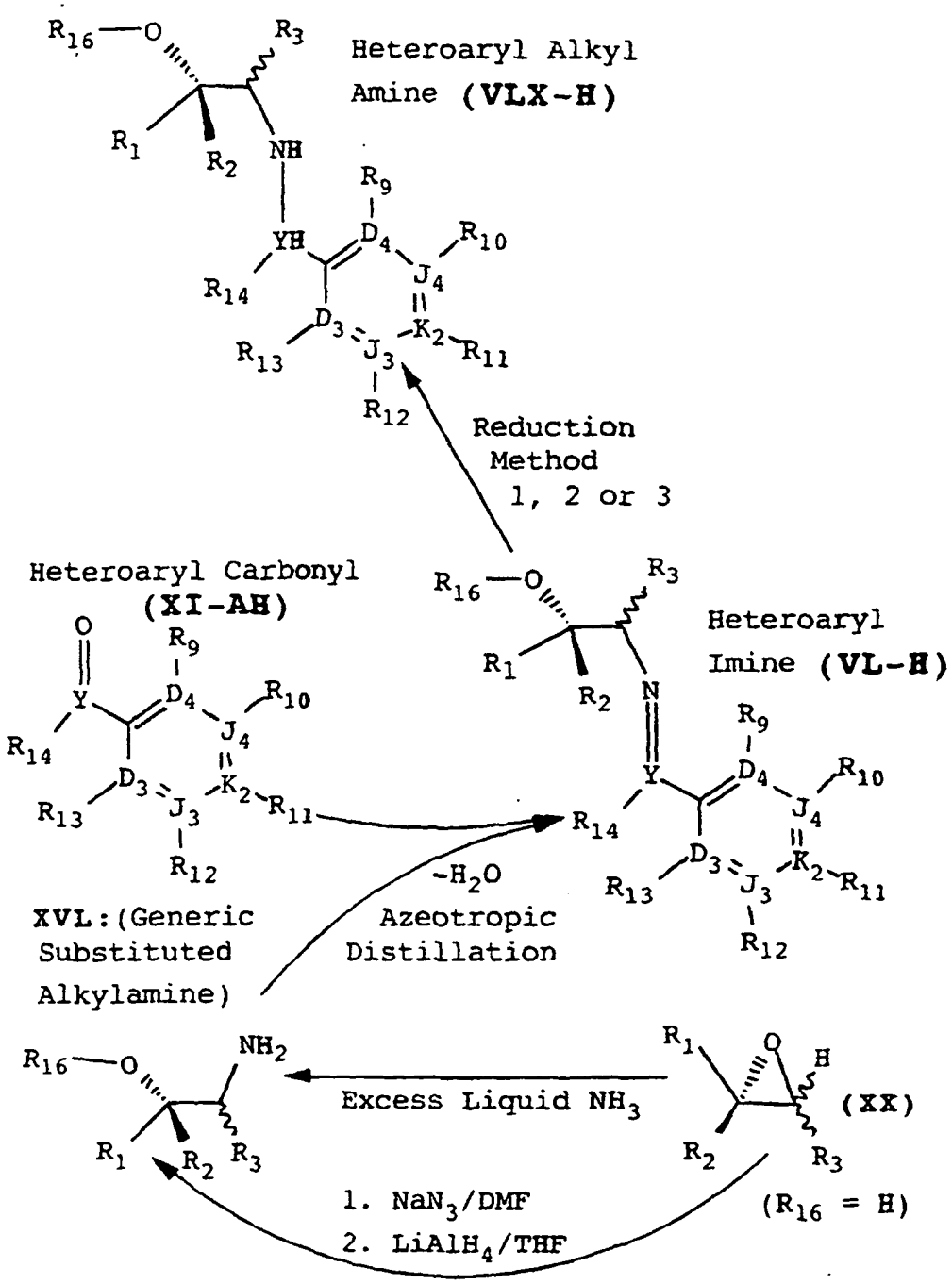
R_{22}-primary or secondary amine
$Pd(dba)_3$/R-(+)-BINAP
2.5 eqiuv. Cs_2CO_3
Toluene/100 °C/1-2 Days



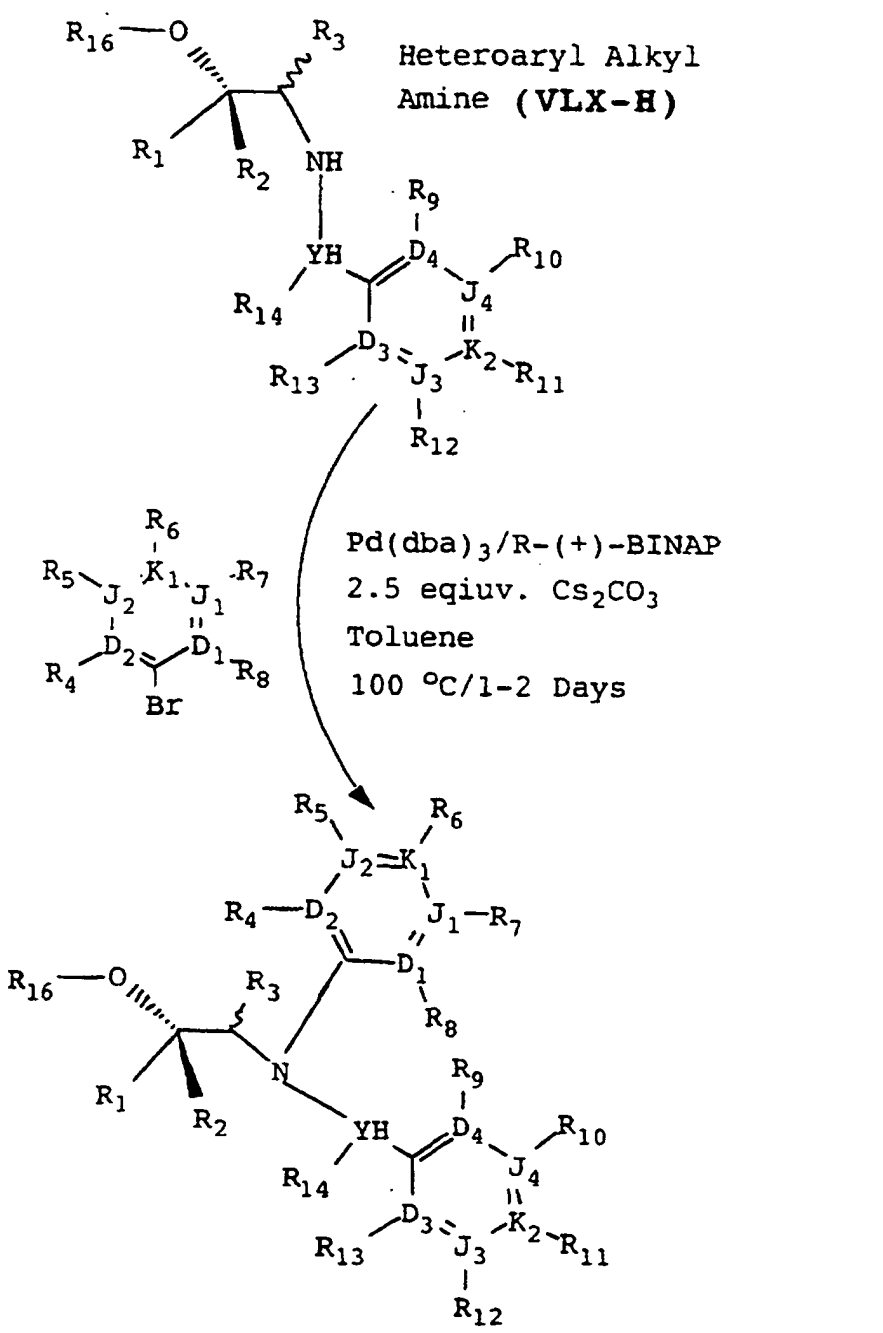
I-CP:(Polycyclic 3-Bromophenyl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

R_{22} is selected independently from any one or two of the following groups: hydrido, hydroxy, aryloxy, alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxyalkyl, aralkoxyalkyl, alkylsulfinylalkyl, haloalkyl, haloalkenyl, halocycloalkyl, halocycloalkoxy, halocycloalkoxyalkyl, arylsulfinylalkyl, arylsulfonylalkyl, alkylamino cycloalkylsulfinylalkyl, cycloalkylsufonylalkyl, heteroarylsulfonylalkyl,heteroarylsulfinylalkyl, aralkylsulfinylalkyl, aralkylsulfonylalkyl, hydroxyalkyl, amino, alkoxy, alkylsulfonylalkyl, aralkylthioalkyl, heteroaralkylthioalkyl, heteroaryloxyalkyl, alkenyloxyalkyl,haloalkoxy, haloalkoxyalkyl, haloalkenyloxyalkyl, heteroaryl, halocycloalkenyloxyalkyl, heteroarylalkyl, aryloxyalkyl, halocycloalkenyl,and heteroarylthioalkyl.

Scheme 9

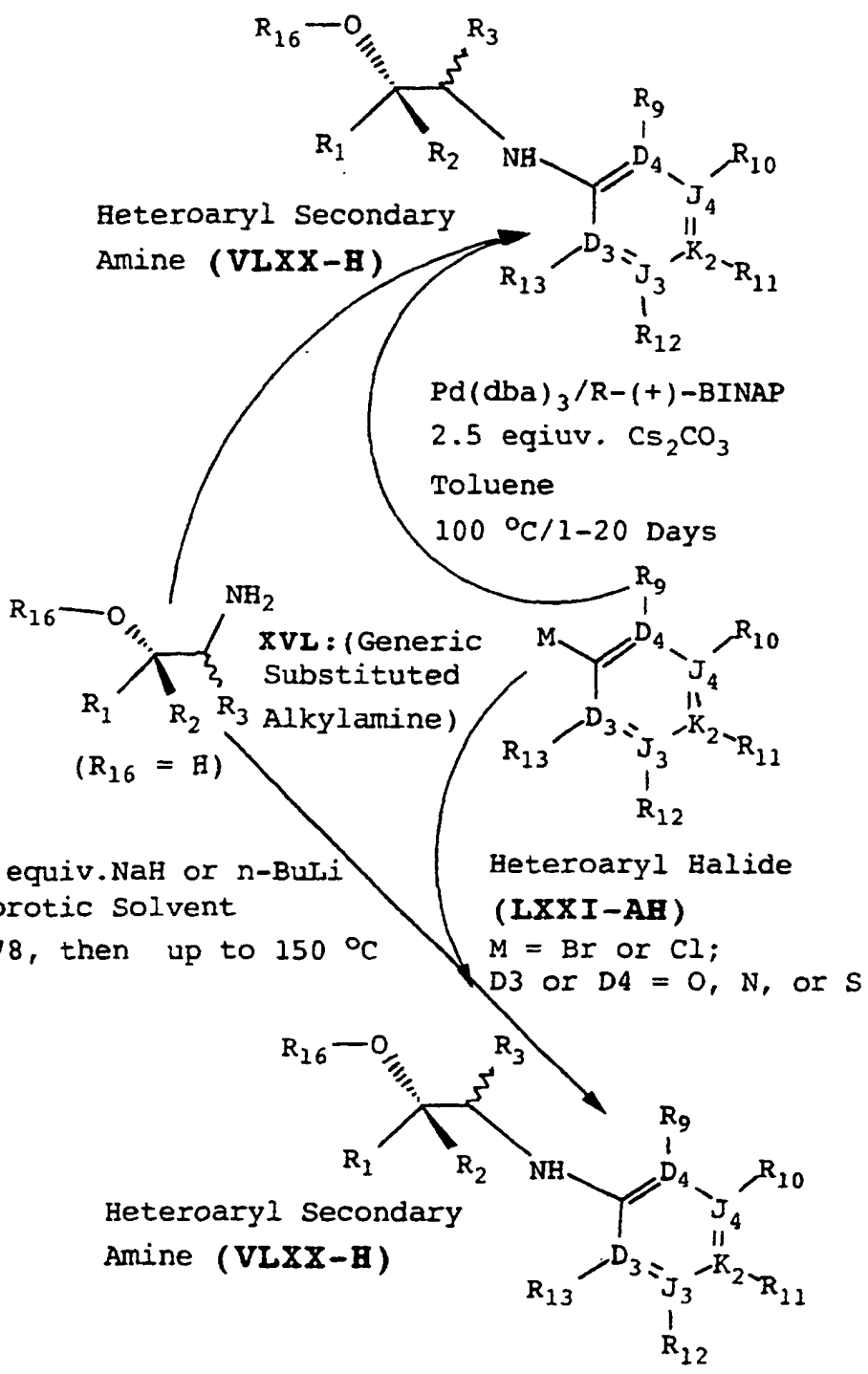

Heteroaryl Alkyl Amine (VLX-H)
Reduction Method 1, 2 or 3
Heteroaryl Carbonyl (XI-AH)
Heteroaryl Imine (VL-H)
XVL: (Generic Substituted Alkylamine)
-H2O Azeotropic Distillation
Excess Liquid NH3
(XX)
1. NaN3/DMF
2. LiAlH4/THF
(R16 = H)

Scheme 10

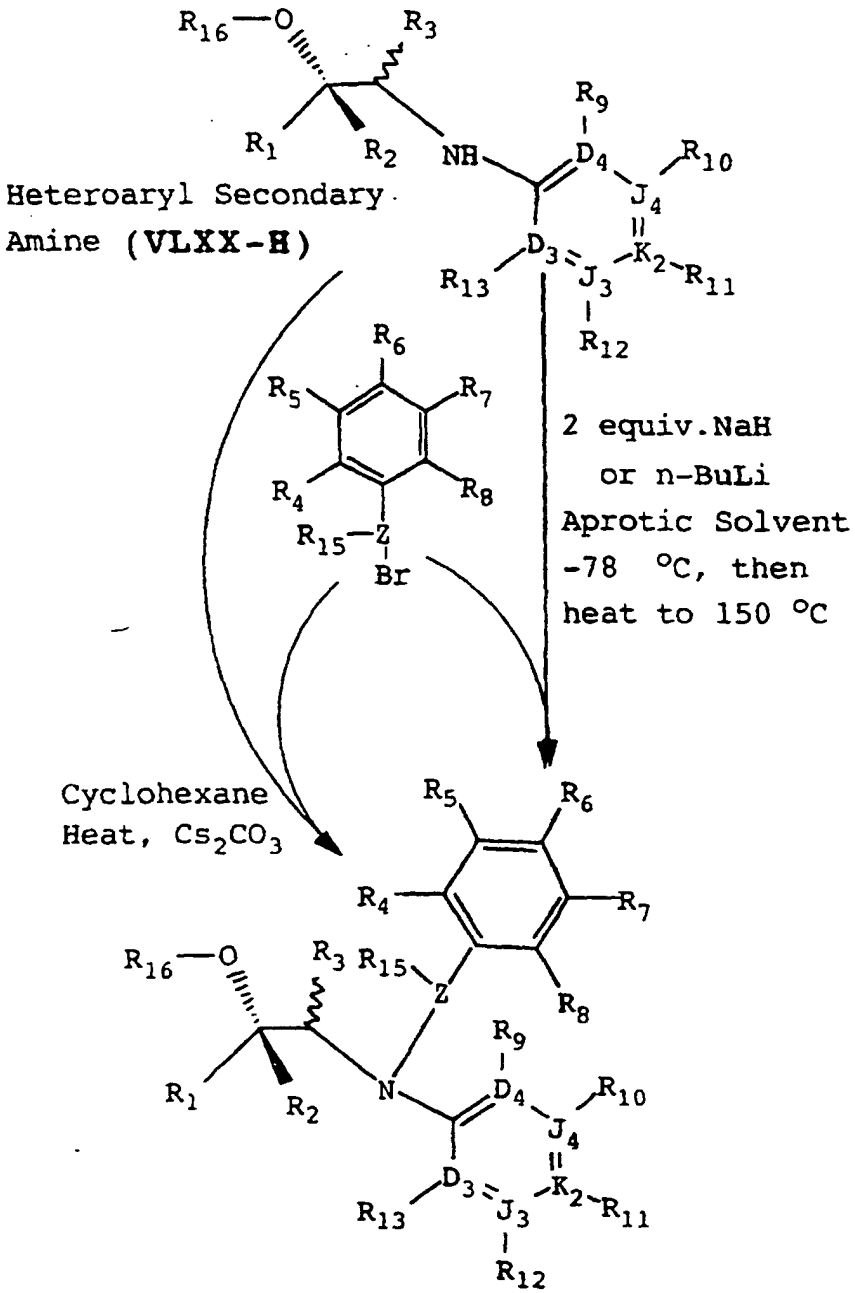


I-HP/I-HPC: (Generic Polycyclic Heteroaryl/Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

Scheme 11


Heteroaryl Secondary Amine (VLXX-H)
Pd(dba)3/R-(+)-BINAP
2.5 eqiuv. Cs2CO3
Toluene
100 °C/1-20 Days
XVL:(Generic Substituted Alkylamine)
(R16 = H)
2 equiv.NaH or n-BuLi
Aprotic Solvent
-78, then up to 150 °C
Heteroaryl Halide
(LXXI-AH)
M = Br or Cl;
D3 or D4 = O, N, or S
Heteroaryl Secondary Amine (VLXX-H)

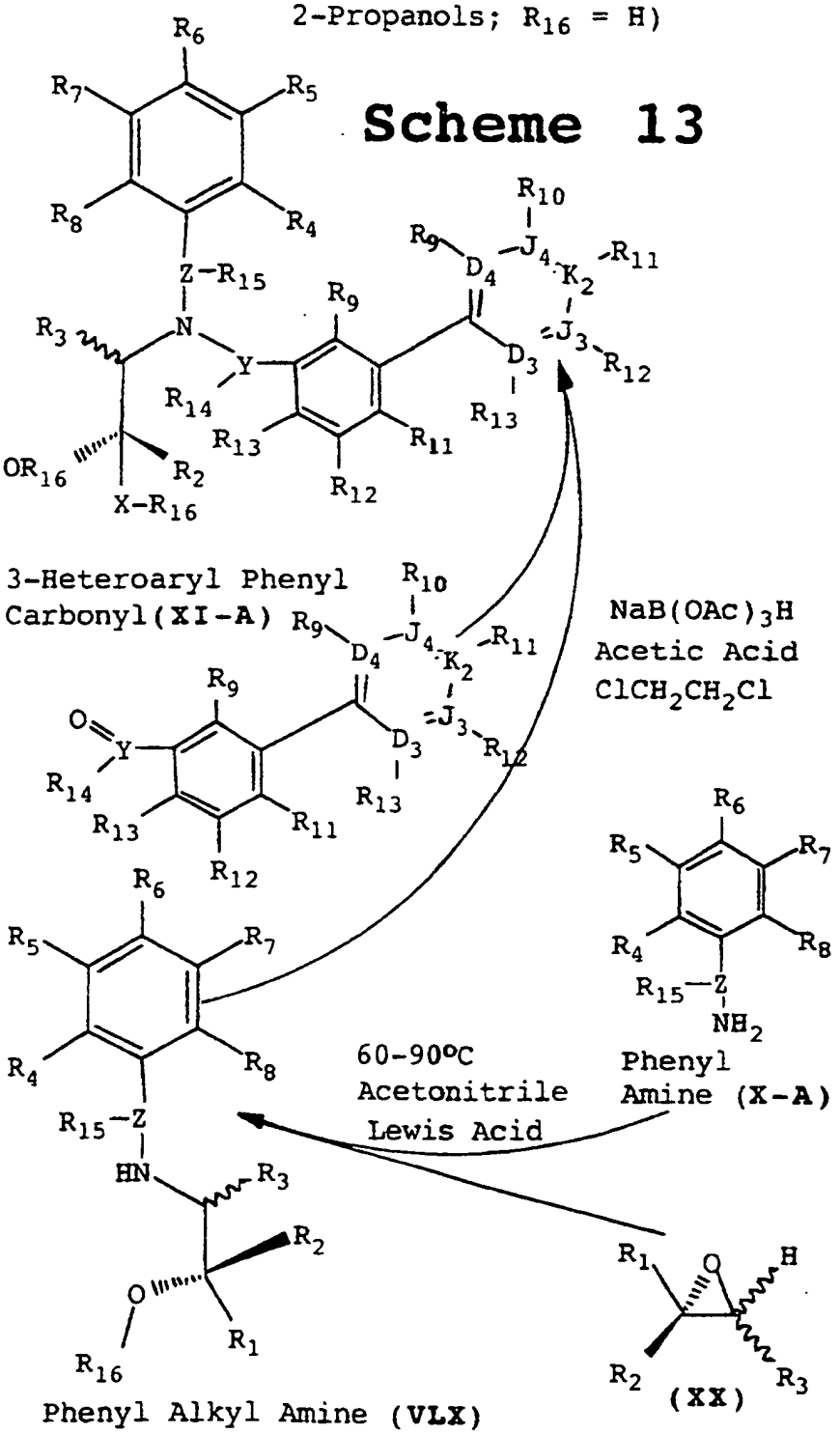
Scheme 12



I-HP/I-HPC/I-CP:(Generic Polycyclic Aryl Aryl and Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols)

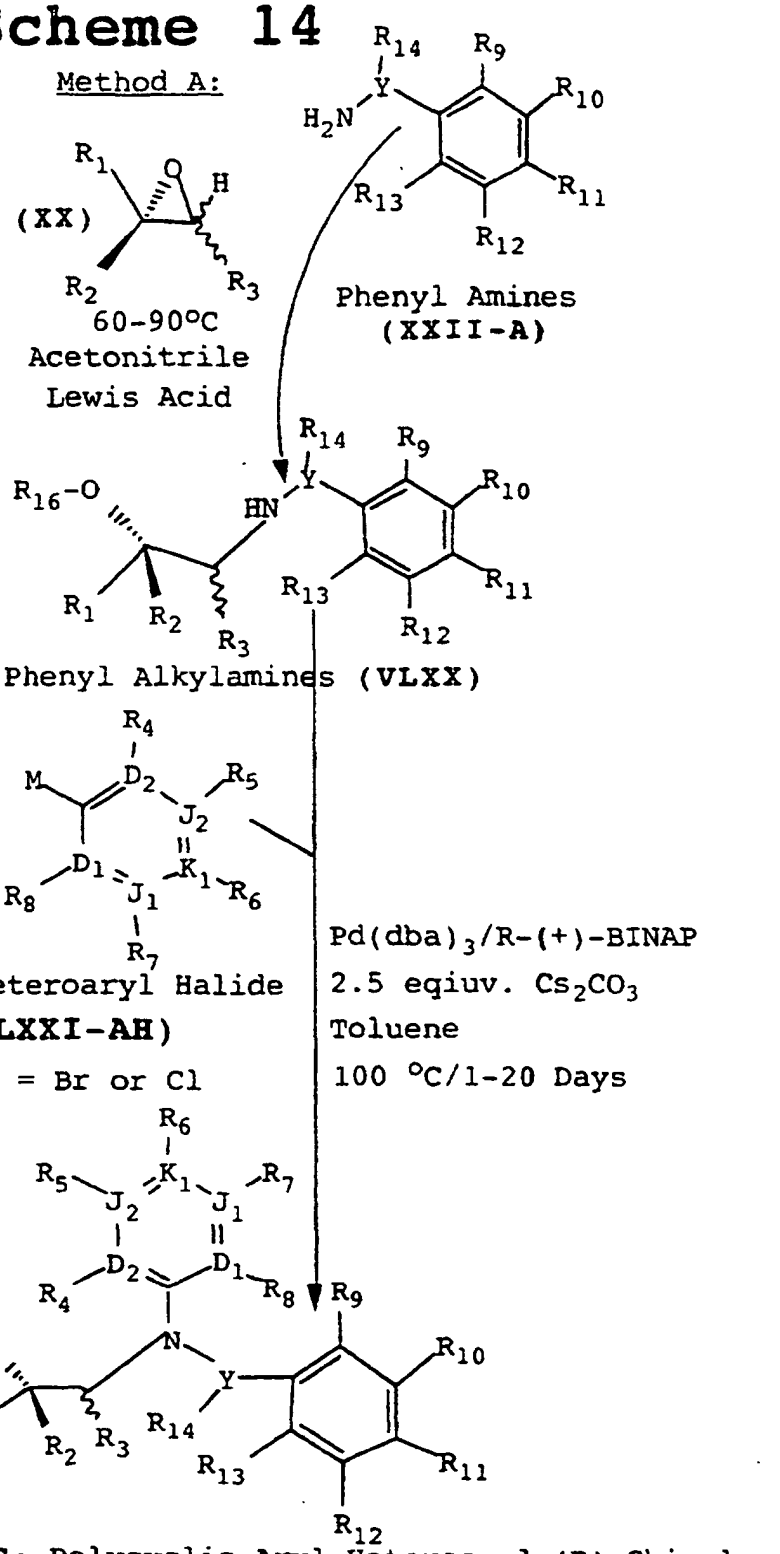
I-CP: (Polycyclic 3-Heteroarylaryl Phenyl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols; R_{16} = H)

Scheme 13



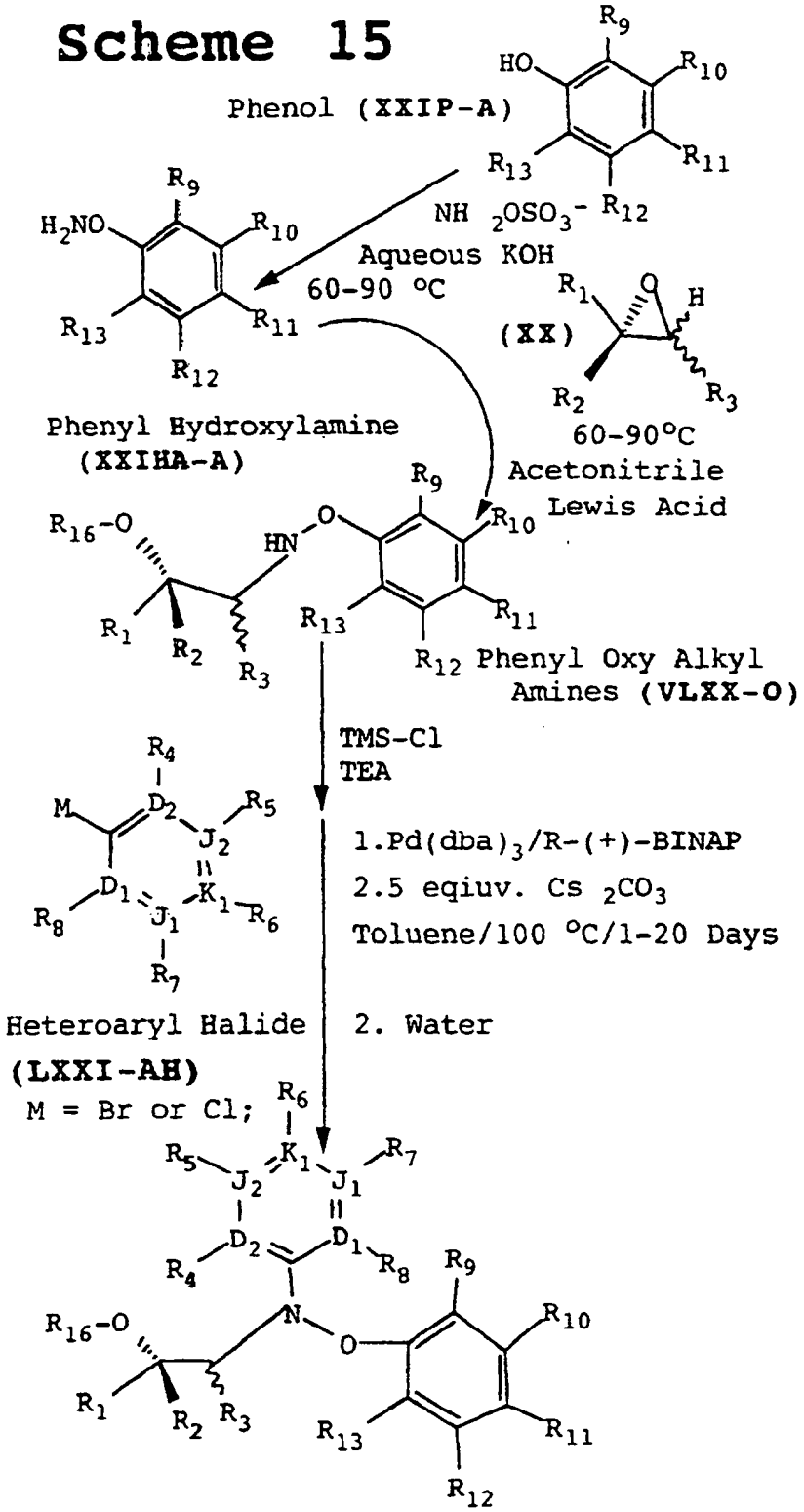
NOTE: HeteroarylAnalogs Can Be Prepared Using Heteroaryl Analogs of **X-A**, **VLX**, and **XI-A**.

Scheme 14



I-HPC: Polycyclic Aryl-Heteroaryl (R)-Chiral Halogenated 1-Substitutedamino-2-Propanols when R_{16} equals H) NOTE: Aryl Analogs **(I-CP)** of **(I-HPC)** Can Be Prepared by Starting With Aryl Bromide Analogs of **(LXXI-AH)**.

Scheme 15



I-HPC: (Polycyclic Heteroaryl-Aryl Phenyl (R)-Chiral Halogenated 1-Substiutedamino-2-Propanols when R_{16} = H and Y = O) NOTE: Diaryl **(I-CP)** and Diheteroaryl **(I-HP)** Analogs Can Be Prepared by Using Aryl Bromide and Heteroaryl-OH, respectively.

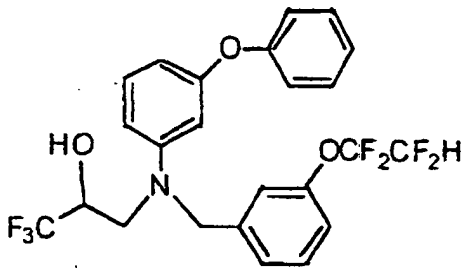
[0171] The following examples are provided to illustrate the present invention and are not intended to limit the scope thereof. Without further elaboration, it is believed that one skilled in the art can, using the preceding descriptions, utilize the present invention to its fullest extent. Therefore the following preferred specific embodiments are to be construed as merely illustrative and not limitative of the remainder of the disclosure in any way whatsoever. Compounds containing multiple variations of the structural modifications illustrated in the preceding schemes or the following Examples are also contemplated. Those skilled in the art will readily understand that known variations of the conditions and processes of the following preparative procedures can be used to prepare these compounds.

[0172] One skilled in the art may use these generic methods to prepare the following specific examples, which have been or may be property characterized by ^{1}H NMR and mass spectrometry. These compounds also may be formed in vivo.

[0173] The following examples contain detailed descriptions of the methods of preparation of compounds of the invention. These detailed descriptions fall within the scope and are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All parts are by weight and temperatures are Degrees centigrade unless otherwise indicated.

EXAMPLE 1

[0174]



(2*R,S*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

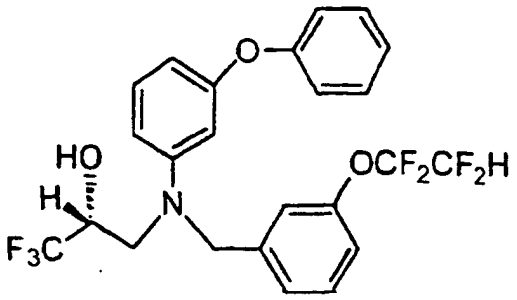
[0175] **EX-1A**) To a solution of 3-(1,1,2,2-tetrafluoroethoxy)toluene (50 g, 0.24 mol) and *N*-bromosuccinimide (42.75 g, 0.24 mol) in 100 mL of carbon tetrachloride under nitrogen was added 2,2'-azobisisobutyronitrile (0.71 g, 0.004 mol). The resultant mixture was refluxed for 2 h, then cooled to room temperature and quenched with 300 mL of water. The organic layer was collected, washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give 66.0 g (96%) of the desired crude 3-(1,1,2,2-tetrafluoroethoxy)bromomethylbenzene product as a yellow oil. ^{1}H NMR indicates that this oil is a mixture of products: 7% dibrominated, 67% monobrominated, and 20% starting material. The crude product was used without further purification. ESMS *m/z* = 287 $[M+H]^+$.

[0176] **EX-1B**) The crude product (56 g, 0.14 mol) from **EX-1A** in 200 mL of cyclohexane was added dropwise under nitrogen to a solution of 3-phenoxyaniline (89 g, 0.480 mol) in 500 mL of cyclohexane. The reaction mixture was refluxed overnight, then cooled to room temperature and diluted with water and diethyl ether. The layers were separated, and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give a dark oil. The crude product was purified by column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to afford 44.96 g (83%) of the desired *N*-(3-phenoxyphenyl)-[[3-(1,1,2,2-tetrafluoroethoxy) phenyl]methyl]amine product as a yellow oil. ESMS *m/z* = 392 $[M+H]^+$.

[0177] To a mixture of the amine product (15.0 g, 0.038 mol) from **EX-1B** and 1,1,1-trifluoro-2,3-epoxypropane (8.58 g. 0.077 mol. TCI) was added a suspension of ytterbium (III) trifluoromethanesulfonate (2.37 g. 0.0031 mol) in 15 mL of acetonitrile. The resulting mixture was heated at 50 °C in a sealed glass vial for 1.5 h. The reaction mixture was cooled to room temperature then diluted with water and ethyl acetate and extracted. The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to afford 12.03 g (62%) of the desired (2*RS*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy) phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol product as a yellow oil. Anal. calcd. for $C_{24}H_{20}F_7NO_3$: C, 57.26; H, 4.00; N, 2.78. Found: C, 56.96; H, 4.35; N, 2.69. HRMS calcd. 504.1410 $[M+H]^+$, found: 504.1431. ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 4H), 7.14 (t, 1H), 7.07, (m, 3H), 7.00 (s, 1H), 6.94 (d, 2H), 6.46 (dd, 1H), 6.38 (dd. 1H), 6.35 (t, 1H), 5.84 (t, 1H), 4.60 (t, 2H), 4.36 (m, 1H), 3.82 (d, 1H), 3.48 (m, 1H), 2.51 1 (s, 1H). ^{19}F NMR ($CDCl_3$) δ -79.0 (s, 3F). -88.21 (d. 2F), -137.05 (dd. 2F).

EXAMPLE 2

[0178]



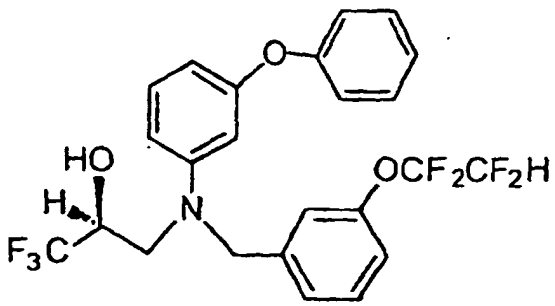
(2*R*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]- 1,1,1-trifluoro-2-propanol

[0179] On a Chiralpak AD HPLC column, (2*RS*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] amino]-1,1,1-trifluoro-2-propanol (12.2 g, 0.024 mol) from **EX-1** was purified by chiral chromatography to give 1.4 g (0.003 mol. 12%) of (2*R*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] amino]-1,1,1-trifluoro-2-propanol as a light yellow oil. Chiral purification was accomplished by eluting with 1:9 isopropanol in heptane at 1.0 mL/min with 250 nm UV detection. The product eluted at 8.43 min. $[\alpha]_{589}$ = +16.8.0 (c 0.125 g/dL, CH_3CN), $[\alpha]_{365}$ = +84.0 (c 0.125, CH_3CN). Anal. calcd. for $C_{24}H_{20}F_7NO_3$: C, 57.26; H, 4.00; N, 2.78. Found: C, 56.96; H, 4.35; N, 2.69. HRMS calcd.: 504.1410 $[M+H]^+$, found: 504.1388. ^1H NMR ($CDCl_3$) δ 7.28 (m, 4H), 7.14 (t, 1H), 7.07, (m, 3H), 7.00 (s, 1H), 6.94 (d, 2H), 6.46 (dd. 1H), 6.38 (dd. 1H), 6.35 (t, 1H), 5.84 (t, 1H), 4.60 (t, 2H), 4.36 (m, 1H), 3.82 (d, 1H), 3.48 (m, 1H), 2.51 (s, 1H). ^{19}F NMR ($CDCl_3$) δ -79.0 (s, 3F), -88.21 (d, 2F), -137.05 (dd, 2F).

EXAMPLE 3

(Included for reference and/or comparison only)

[0180]

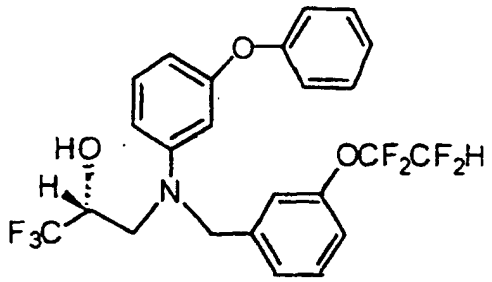


(2S)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0181] On a Chiralpak AD HPLC column. (2*RS*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] amino]-1,1,1-trifluoro-2-propanol (12.2 g, 0.024 mol) from **EX-1** was purified by chiral chromatography to give 10.5 g (0.021 mol, 86%) of (2*S*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propanol as a light yellow oil. Chiral purification was accomplished by eluting with 1:9 isopropanol in heptane at 1.0 mL/min with 250 nm UV detection. The product eluted at 6.36 min. $[\alpha]_{589}$ = -17.0 (c 0.265 g/dL, CH_3CN), $[\alpha]_{365}$ = -85.7 (c 0.265, CH_3CN). Anal. calcd. For $C_{24}H_{20}F_7NO_3$: C, 57.26; H, 4.00; N, 2.78. Found: C, 56.96; H, 4.35; N, 2.69. HRMS calcd.: 504.1410 $[M+H]^+$, found: 504.1431. ^1H NMR ($CDCl_3$) δ 7.28 (m, 4H), 7.14 (t, 1H), 7.07, (m, 3H), 7.00 (s, 1H), 6.94 (d, 2H), 6.46 (dd, 1H), 6.38 (dd, 1H), 6.35 (t, 1H), 5.84 (t, 1H), 4.60 (t, 2H), 4.36 (m, 1H), 3.82 (d, 1H), 3.48 (m, 1H), 2.51 (s, 1H). ^{19}F NMR ($CDCl_3$) δ -79.0 (s, 3F), -88.21 (d, 2F), - 137.05 (dd. 2F).

EXAMPLE 4

[0182]



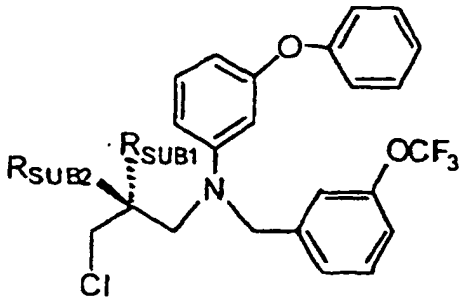
(2*R*)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0183] Using a procedure adopted from H.C.Brown et al. (*J. Org. Chem.* **60**, 41-46. (1995)). *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane was prepared beginning with the transfer of (+)-*B*-chlorodiisopinocampheylborane ((+)-DIP-Cl, 1.2 kg, 3.74 mol) to a 5 L three neck flask containing 5 L of ether under nitrogen. Anhydrous ether (5 L) was added. and the mixture was stirred until the solids dissolved and the temperature equilibrated to 0 °C. Then 3-bromotrifluoroacetone (326 mL, 3.14 mol) was added. and the reaction was stirred for 72 h while maintaining the temperature between -4 and +5 °C. The reaction was followed by ^{19}F NMR by removing an aliquot (20 µL), quenching with anhydrous methanol (0.6 mL), and referencing to external D_2O. The reduction was 68 % complete after 48 h. The ether was removed under vacuum (100 torr to 0.1 torr), leaving a pale, viscous oil. A 5 L 3-neck flask equipped with stirrer. dropping funnel, and short-path distillation head with chilled receiver was charged with 50% (w/w) aqueous NaOH and heated to 40 °C. With external heat removed. the quenched reduction mixture was added dropwise to the aqueous NaOH, with the rate controlled to maintain the pot temperature below 65 °C. The product epoxide formed immediately, distilling over with a head temperature of 32-42 °C. A yellow-orange solid byproduct was broken up by stirring and some foaming was observed. When the distillation was complete. 145 g (43%) of the desired *R*-(+)-1,1,1-trifluoro-2,3-epoxy-propane product was obtained as a clear, colorless oil. ^1H NMR (C_6D_6) δ 2.50 (m, 1H, CF_3CH), 2.15 (dd, 1H, J = 2.10, 5.01 Hz), 1.75 (m, 1H). ^{19}F NMR (C_6D_6) δ -75.4 (d, J = 4.7 Hz). Chiral GC/MS analysis was performed on the corresponding diethylamine adduct using a gamma cyclodextrin column (Supelco gammadex120 G-cyclodextrin fused silica): 4 drops of the epoxide, *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane, and 4 drops of diethylamine were heated briefly in a sealed vial, cooled. diluted with methyl *t*-butyl ether, and analyzed. Found: two gc peaks: 10.97 min and 11.11 min (ratio 1: 230; 99% ee), where the *R*-product predominated. MS calcd. for $C_7H_{14}F_3NO$: *m/z* = 186 $[M+H]^+$, found: 186. for both gc peaks. In contrast, the diethylamine adduct obtained with the TCI trifluoromethyl-oxirane (lot OGH01) from **EX-1**, gave 2 peaks with identical MS signals *m/z* = 186, 10.96 min and 11.12 min (ratio 8.5:1; 79% ee), where the *S*-product predominated.

[0184] To a mixture *N*-(3-phenoxyphenyl)-[[3-(1,1,2,2-tetrafluoroethoxy)phenyl] methyl]-amine from **EX-1B** (1.48 g, 0.0038 mol) and *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.64 g, 0.0057 mol) was added a suspension of ytterbium (III) trifluoro-methanesulfonate (0.23 g, 0.0004 mol) in 1.5 mL of acetonitrile. The resulting mixture was heated at 50 °C in a sealed glass tube for 1.5 h. The reaction mixture was cooled to room temperature then diluted with water and ethyl acetate and extracted. The organic layers were combined, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to afford 1.2 g (63%) of the desired (2*R*)-3-[(3-phenoxyphenyl)-[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol product as a pure yellow oil (>96% ee by chiral HPLC analysis), which was identical in all respects to **EX-2.** Anal. calcd. for $C_{24}H_{20}F_7NO_3$: C, 57.26; H, 4.00; N, 2.78. found: C, 56.96; H, 4.35; N, 2.69. HRMS calcd.: 504.1410 $[M+H]^+$. found: 504.1431. ^1H NMR ($CDCl_3$) δ 7.28 (m, 4H), 7.14 (t, 1H), 7.07, (m. 3H), 7.00 (s, 1H), 6.94 (d, 2H), 6.46 (dd, 1H), 6.38 (dd, 1H), 6.35 (t, 1H), 5.84 (t, 1H), 4.60 (t, 2H), 4.36 (m, 1H), 3.82 (d, 1H), 3.48 (m, 1H), 2.51 (s, 1H), ^{19}F NMR ($CDCl_3$) δ -79.0 (s, 3F), -88.21 (d, 2F), -137.05 (dd, 2F).

[0185] Additional examples can be prepared by one skilled in the art using similiar methods and commercially available epoxides. For example, 3-[(3-phenoxyphenyl)[[3-(trifluoromethoxy)phenyl]methyl]amino]-1-chloro-2-propanols can be prepared from the reaction of *N*-(3-phenoxyphenyl)-[[3-(trifluoromethoxy)phenyl]methyl]amine with either (*R*)-epichlorohydrin or (*S*)-epichlorohydrin, as illustrated in Example Table 1.

Example Table 1. 3-[(3-phenoxyphenyl)[[3-(trifluoromethoxy)phenyl]methyl]amino]-1-chloro-2-propanols.

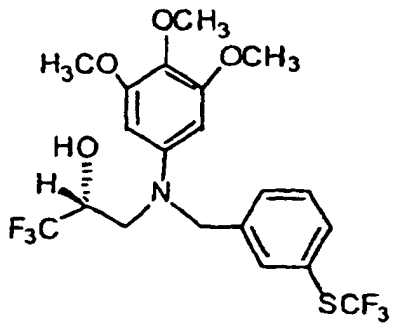


Ex. No.	R_{SUB1}	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
5	OH	H	452.1240	452.1245
6*	H	OH	452.1240	452.1259

*Included for reference and/or comparison only.

EXAMPLE 7

[0186]



(2*R*)-3-[(3,4,5-trimethoxyphenyl)[[3-(trifluoromethylthio)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

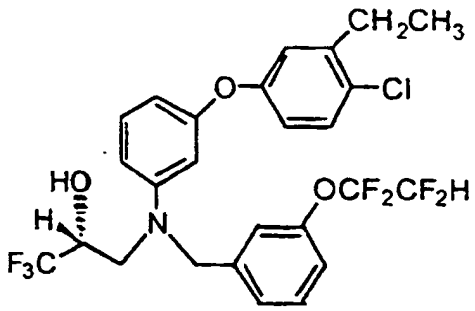
[0187] **EX-45A)** To a 1,2-dichloroethane (12 mL) solution of 3,4,5-trimethoxyaniline (0.80 g, 4.4 mmol) was added (3-trifluoromethylthio)benzaldehyde (0.90 g, 4.4 mmol), $NaB(OAc)_3H$ (1.20 g, 5.66 mmol) and acetic acid (0.26 mL, 4.5 mmol). The cloudy solution was stirred at room temperature for 1 h. The reaction mixture was poured into water and extracted with dichloromethane. The organic layer was washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated to give 1.58 g (96%) of the desired *N*-(3,4,5-trimethoxyphenyl)[[3-trifluoromethylthiophenyl]methyl] amine product as an off-white solid. MS: *m/z* = 373.8 $[M+H]^+$.

[0188] To an acetonitrile (3.2 mL) solution of amine (1.20 g, 32 mmol) from **EX-45A** was added *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.55 mL 6.4 mmol) from **EX-4** and $Yb(OTf)_3$ (0.40 g, 0.64 mmol). The cloudy solution was stirred in a sealed flask at 50 °C for 18 h. The cooled reaction mixture was diluted with diethyl ether and washed with water and brine. The organic layer was dried ($MgSO_4$) and evaporated to an oil. Purification by flash column chromatography

on silica gel eluting with 20% ethyl acetate in hexane gave an oil which was triturated with hexanes to give a white solid. The precipitate was isolated by filtration and dried *in vacuo* to give 0.82 g (53 %) of the desired (2*R*)-3-[(3,4,5-trimethoxyphenyl)[[3-(trifluoromethylthio)phenyl]methyl]-amino]-1,1,1-trifluoro-2-propanol product as a white solid. m.p. 88.9-89.1 °C (95% ee by chiral HPLC). Anal. calcd. for $C_{20}H_{21}NO_4SF_6$: C. 49.48; H, 4.36; N, 2.89. Found: C, 49.29; H, 4.21; N, 2.81. HRMS calcd.: 486.1174 $[M+H]^+$, found: 486.1158. ^1H NMR (C_6D_6) δ 3.10 (d, 1H), 3.18 (dd, 1H), 3.32 (s, 6H), 3.53 (d, 1H), 3.64 (s, 3H), 4.01 (m, 1H), 4.21 (dd, 2H), 5.70 (s, 2H), 6.80 (t, 1H), 6.94 (d, 1H), 7.23 (d, 1H), 7.37 (s, 1H). $[\alpha]_{589}$ = +26.8 (c 1.099 g/dL, $CHCl_3$).

EXAMPLE 8

[0189]



(2*R*)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0190] **EX-8A)** To a solution of 1.3-dinitrobenzene (16.8 g. 0.1 mol) and 4-chloro-3-ethylphenol (15.6 g. 0.1 mol) in 200 mL of dimethylsulfoxide was added cesium carbonate (65 g, 0.2 mol). The reaction mixture was heated at 100 °C under nitrogen overnight then cooled to room temperature. The reaction mixture was filtered through celite then rinsed with diethyl ether and a small amount of water. The filtrate was extracted several times with diethyl ether. The organic layers were combined. washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give 21.8 g (78%) of the desired 3-(4-chloro-3-ethylphenoxy)-1-nitrobenzene product as a dark orange oil, which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd. for $C_{14}H_{12}ClNO_3$: 295.0849 $[M+NH_4]^+$, found 295.0862.

[0191] **EX-8B**) To a solution of 3-(4-chloro-3-ethylphenoxy)-1-nitrobenzene (10 g, 0.036 mol) from **EX-8A** in 400 mL of glacial acetic acid and 1 mL of water was added zinc metal (20 g, 0.305 mol) at room temperature, and the resultant mixture was stirred for 1 h. The reaction mixture was filtered through celite. The filtrate was neutralized with ammonium hydroxide and extracted with diethyl ether. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give 10 g (100%) of the desired 3-(4-chloro-3-ethylphenoxy)aniline product as a dark orange oil, which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd. for $C_{14}H_{14}ClNO$: 248.0842 $[M+H]^+$, found: 248.0833.

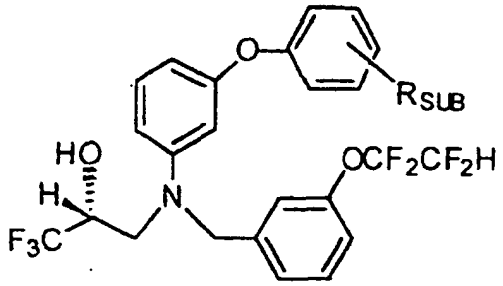
[0192] **EX-8C**) To a solution of 3-(4-chloro-3-ethylphenoxy)aniline (2.0 g, 8.1 mmol) from **EX-8B** and 3-(1,1,2,2-tetrafluoroethoxy)benzaldehyde (1.6 g. 7.3 mmol) in 30 mL of dichloroethane was added sodium triacetoxyborohydride (2.0 g, 9.7 mmol) and glacial acetic acid (0.51 mL. 8.9 mmol). The reaction mixture was stirred at room temperature for 1 h then quenched with water and extracted with diethyl ether. The organic layer was washed with water and brine. dried over $MgSO_4$, and concentrated *in vacuo* to give 3.5 g (95%) of the desired *N*-[(4-chloro-3-ethylphenoxy)phenyl]-3-[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] amine product as a brown oil, which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd, for $C_{23}H_{20}ClF_4NO_2$: 454.1197 $[M+H]^+$, found: 454.1220.

[0193] A solution of *N*-[(4-chloro-3-ethylphenoxy)phenyl]-3-[[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]methyl]amine (1.8 g, 4.0 mmol) from **EX-8C**, *R*-(+)-1,1,1-trifluoro-2,3-epoxy-propane (0.64 g, 0.0057 mol) from **EX-4**, and ytterbium (III) trifluoromethanesulfonate (0.25 g, 0.4 mmol) in 1.5 mL of acetonitrile was heated at 40 °C in a sealed glass tube for 1 h. The reaction mixture was cooled to room temperature then diluted with water and diethyl ether and extracted. The ether layer was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* The crude product was purified by column chromatography on silica gel eluting with 1:7:0.01 of ethyl acetate:hexane:ammonium hydroxide to afford 1.5 g (66%) of the desired (2*R*)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl] methyl]amino]-1,1,1-tri-fluoro-2-propanol product as a yellow oil (96% ee by chiral HPLC analysis). $[\alpha]_{589}^{25}$ = + 36.9 (c 1.044g%, $CHCl_3$). $[\alpha]_{365}^{25}$ = + 189.7 (c 1.044g%, $CHCl_3$). The refractive index @ 25 °C is 1.5275. Anal. calcd. for

$C_{26}H_{23}ClF_7NO_3$: C, 55.18; H, 4.10; N, 2.48. found: C, 54.92; H, 4.05; N, 2.33. HRMS calcd.: 566.1330 $[M+H]^+$, found: 566.1323. ^1H NMR ($CDCl_3$) δ 7.30 (t, 1H), 7.20 (d, 1H), 7.15 (t, 1H), 7.08 (t, 2H). 7.00 (s, 1H), 6.86 (d, 1H), 6.68 (dd, 1H), 6.48 (dd, 1H), 6.36 (dd, 1H), 6.34 (t, 1H), 5.81 (tt, 1H), 4.62 (s, 2H), 4.32 (m, 1H), 3.84 (dd, 1H), 3.55 (dd, 1H), 2.67 (q, 2H), 2.45 (bs, 1H), 1.17 (t, 3H).^{19}F NMR ($CDCl_3$) δ -79.22 (d, 3F), -88.57 (m, 2F), -137.16 (dt, 2F).

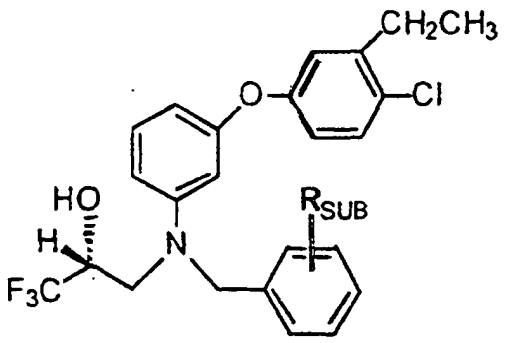
[0194] Additional examples of (2*R*)-3-[[3-(substituted-phenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanols and (2*R*)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-substituted-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanols can be prepared by one skilled in the art using similar methods, as shown in Example Tables 2 and 3, respectively.

Example Table 2. (2*R*)-3-[[3-(Substituted-phenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
9	4-methyl	518.1566	518.1587
10	3-isopropyl	546.1879	546.1900
11	3-ethyl	532.1723	532.1713

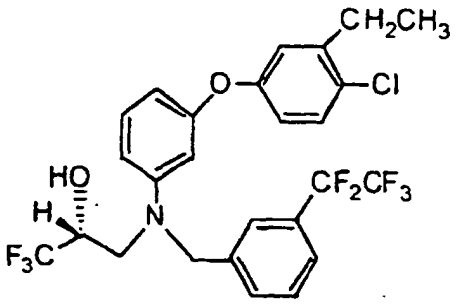
Example Table 3. (2*R*)-3-[[3-(4-Chloro-3-ethylphenoxy)phenyl][[3-substituted-phenyl]methyl]amino]-1.1.1-trifluoro-2-propanols.



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
12	3-trifluoromethoxy	534.1271	534.1309
13	3-trifluoromethyl, 4-fluoro	536.1228	536.1265
14	2-fluoro, 4-trifluoromethyl	536.1228	536.1241
15	2-trifluoromethyl, 4-fluoro	536.1228	536.1245
16	2-fluoro, 5-trifluoromethyl	536.1228	536.1252
17	2-fluoro, 6-trifluoromethyl	536.1228	536.1199

EXAMPLE 18

[0195]



(2*R*)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[13-(1,1,1,2,2-pentafluoroethyl)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0196] **EX-18A**) Sodium pentafluoroethyl propionate (8.4 g, 50 mmol) and 3-iodotoluene (5.5 g, 25 mmol) were dissolved in anhydrous DMF (300 mL) under nitrogen. CuI (9.5 g, 50 mmol) was added, and the mixture was heated to 160 °C under nitrogen for 4 h, at which time a 15 mL fraction of a mixture of DMF and 3-pentafluoroethyl toluene was collected. The distillate was diluted with Et_2O and was washed with brine. The ether layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give 5.25 g (55%) of the desired 3-pentafluoroethyl-toluene product as a colorless oil. ^1H NMR ($CDCl_3$) δ 7.36 (m, 4H), 2.40 (s, 3H). ^{19}F NMR ($CDCl_3$) δ -85.2 (s, 3F), -115.2 (s, 2F).

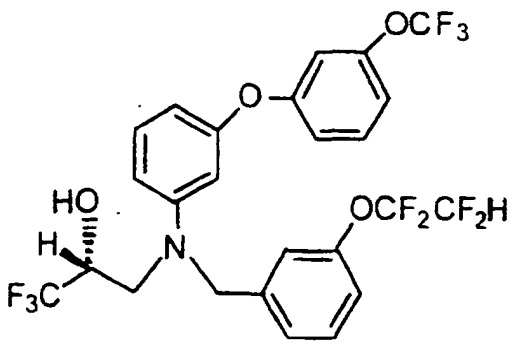
[0197] **EX-18B**) The 3-pentafluoroethyl-toluene (2.9 g, 13.8 mmol) product from **EX-18A** and *N*-bromosuccinimide (2.5 g, 13.8 mmol) were dissolved in CCl_4 (25 mL). AIBN (50 mg, 0.3 mmol) was added, and the mixture was refluxed for 3.5 h under N_2. The reaction mixture was cooled to room temperature and diluted with water. The layers were separated, and the organic layer was washed with brine, dried with anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give 3.4 g (87%) of a colorless oil. The ^1H NMR spectrum indicated that the crude product contained 3-pentafluoroethyl-benzylbromide (70%), the benzyldibromide (10%) and pentafluoroethyl toluene (20%). ^1H NMR ($CDCl_3$) δ 7.60 (m. 2H), 7.50 (m, 2H), 4.50 (s, 2H). ^{19}F NMR ($CDCl_3$) δ -85.1 (s, 3F), -115.4 (s, 2F).

[0198] **EX-18C**) A solution of 3-(4-chloro-3-ethylphenoxy)aniline (1.7 g. 6.9 mmol) was prepared in cyclohexane (13 mL). A solution of crude 3-pentafluoroethyl benzylbromide (1g, 3.5 mmol) product from **EX-18B** in cyclohexane (10 mL) was added dropwise under nitrogen over 3 min. The reaction mixture was refluxed under N_2 for 24 h and then was cooled to room temperature. The mixture was diluted with Et_2O and saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried with anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by chromatography on silica gel eluting with hexanes in ethyl acetate (95:5) which gave 0.56 g (35%) of the desired *N*-[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(pentafluoro-ethyl)phenyl]methyl]amine product as a brown oil. ^1H NMR ($CDCl_3$) δ 7.53 (m, 4H), 7.27 (d, 1H), 7.15 (t, 1H), 6.93 (d, 1H), 6.77 (dd, 1H), 6.41 (tt, 2H), 6.30 (t, 1H), 4.41 (s, 2H), 2.73 (q, 2H), 1.23 (t, 3H). ^{13}C NMR ($CDCl_3$) δ 158.6, 156.1, 143.4, 141.3, 140.2, 131.3, 130.7, 130.4, 129.4, 128.1, 120.4, 117.8, 108.8. 103.9, 48.5, 27.5, 14.1. ^{19}F NMR ($CDCl_3$) δ -85.1 (s, 3F), -115.2 (s, 2F). HRMS calcd. for $C_{23}H_{19}ClF_5NO$: 456.1154 $[M+H]^+$, found: 456.1164.

[0199] The *N*-[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(pentafluoroethyl)phenyl]-methyl]amine (0.4 g, 0.88 mmol) product of **EX-18C** was dissolved in anhydrous acetonitrile (1.5 mL). *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.22 g, 1.94 mmol) and $Yb(OTf)_3$ (22 mg, 0.035 mmol) were added. and the reaction mixture was stirred under N_2 at 45 °C in a sealed glass tube for 15 h. The reaction mixture was then cooled to room temperature and diluted with Et_2O and saturated aqueous $NaHCO_3$. The layers were separated and the aqueous layer was extracted with Et_2O. The ether layers were combined, washed with brine, dried with anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The viscous oil was adsorbed onto silica gel and purified by column chromatography eluting with hexanes in ethyl acetate (95:5) which gave 0.32 g (64%) of the desired (2R)-3-[(4-chloro-3-ethylphenoxy)phenyl[[3-(pentafluoroethyl)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol product as a viscous. colorless oil. ^1H NMR ($CDCl_3$) δ 7.47 (m. 4H), 7.23 (m. 3H), 6.90 (d, 1H), 6.72 (dd, 1H), 6.52 (d, 1H), 6.42 (m, 2H), 4.73 (s, 2H), 4.39 (m, 1H), 3.91 (dd, 1H), 3.58 (m, 2H), 2.73 (q, 2H), 2.57 (s, 1H), 1.22 (t, 3H). ^{19}F NMR ($CDCl_3$) δ -79.2 (s, 3F), -84.9 (s, 3F), -115.2 (s, 2F). HRMS calcd. for $C_{26}H_{22}ClF_8NO_2$: 568.1290 $[M+H]^+$, found: 568.1296.

EXAMPLE 19

[0200]



(2*R*)-3-[[3-(3-trifluoromethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0201] **EX-19A**) To a solution of 1,3-dinitrobenzene (4.5 g, 0.03 mol) and 3-trifluoromethoxy-phenol (4.8 g, 0.03 mol) in 54 mL of dimethylsulfoxide was added cesium carbonate (21.8 g, 0.07 mol). The reaction mixture was heated at 100 °C under nitrogen overnight then cooled to room temperature. The reaction mixture was diluted with water and extracted with diethyl ether several times. The organic layers were combined, washed with 1 N HCl and water. dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:9 ethyl acetate in hexane to afford 3.0 g (38%) of the desired 3-(3-trifluoro-methoxyphenoxy)nitrobenzene product as a yellow-orange liquid which was 85% pure by reverse phase HPLC analysis. This material was carried on without further purification.

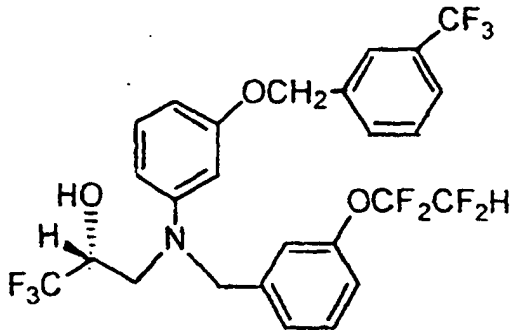
[0202] **EX-19B**) To a solution of 3-(3-trifluoromethoxyphenoxy)nitrobenzene (3.0 g, 0.01 mol) from **EX-19A** in 100 mL of glacial acetic acid was added zinc metal (6.6 g, 0.1 mol) at room temperature, and the resultant mixture was stirred for 1 h. The reaction mixture was filtered through celite. The filtrate was neutralized with ammonium hydroxide and extracted with diethyl ether then ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:9 ethyl acetate in hexane to afford 1.2 g (44%) of the desired 3-(3-trifluoromethoxyphenoxy)aniline product as a yellow oil which was 98% pure by reverse phase HPLC analysis. Anal. calcd. for $C_{13}H_{10}F_3NO_2$: C, 58.00; H, 3.74: N, 5.20. found: C, 57.68; H, 3.57; N, 5.14. HRMS calcd.: 270.0742 $[M+H]^+$, found: 270.0767.

[0203] **EX-19C)** To a solution of 3-(3-trifluoromethoxyphenoxy)aniline (1.0 g. 3.7 mmol) from **EX-19B** and 3-(1,1,2,2-tetrafluoroethoxy)benzaldehyde (0.83 g. 3.7 mmol) in 18.5 mL of dichloroethane was added sodium triacetoxyborohydride (1.0 g, 4.7 mmol) and glacial acetic acid (0.25 mL, 4.3 mmol). The reaction mixture was stirred at room temperature overnight then quenched with saturated aqueous sodium bicarbonate and extracted with methylene chloride. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* to give 1.8 g (100%) of the desired [3-(3-trifluoromethoxy-phenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl] amine product as a yellow oil. which was greater than 90% pure by reverse phase HPLC analysis. HRMS calcd. for $C_{22}H_{16}F_7NO_3$: 476.1097 $[M+H]^+$, found: 476.1069. This material was carried on to the next step without further purification.

[0204] A solution of [3-(3-trifluoromethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]methyl]amine (1.8 g, 3.7 mmol) from **EX-19C,** *R*-(+)-1,1,1-trifluoro-2,3-epoxy-propane (0.57 g, 5.2 mmol), and ytterbium (III) trifluoromethanesulfonate (0.24 g, 0.38 mmol) in 2.0 mL of acetonitrile was heated at 40 °C in a sealed glass tube overnight. At this time reverse phase HPLC analysis indicated that the reaction was only 50% complete. Additional ytterbium (III) trifluoromethanesulfonate and *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.26 g. 2,3 mmol) were added to the reaction mixture and again heated at 40 °C in a sealed glass tube for 48 h. The reaction mixture was cooled to room temperature then diluted with water and methylene chloride and extracted. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by reverse phase HPLC eluting with 30% to 90% acetonitrile in water to afford 1.25 g (23%) of the desired (2*R*)-3-[[3-(3-trifluoromethoxyphenoxy) phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol product as yellow-brown oil (90% ee by chiral HPLC analysis). HRMS calcd. for $C_{25}H_{19}F_{10}NO_4$: 588.1233 $[M+H]^+$, found: 588.1225, ^1H NMR ($CDCl_3$) δ 7.35-7.18 (m, 3H), 7.12 (t, 2H), 7.01 (s, 1H), 6.93 (d, 1H), 6.85 (d, 1H), 6.82 (s, 1H), 6.56 (dd, 1H), 6.47 (dd, 1H), 6.41 (s, 1H), 5.88 (t, 1H), 4.66 (s, 2H), 4.35 (m, 1H), 3.86 (d, 1H), 3.59 (dd, 1H), 2.02 (s, 1H). ^{19}F NMR ($CDCl_3$) δ -58.31 (s, 3F), -79.24 (d, 3F), -88.57 (m. 2F), - 137.16 (dt. 2F).

EXAMPLE 20

[0205]



(2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoromethyl)-phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol

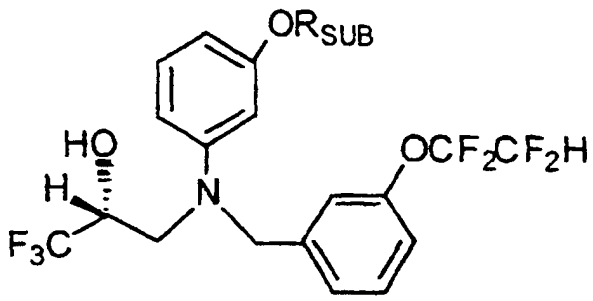
[0206] **EX-20A**) To a solution of 3-aminophenol (4.91 g. 45.0 mmol) and 3-(1,1,2.2-tetrafluoroethoxy)benzaldehyde (10.0 g, 45.0 mmol) in 100 mL of 1,2-dichloroethane was added sodium triacetoxyborohydride (14.28 g 67.5 mmol) and glacial acetic acid (2.7 mL. 47.3 mmol). The reaction mixture was stirred at room temperature for 6 h then quenched with water and extracted with dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate, dried over $MgSO_4$, and concentrated *in vacuo* to give 11.82 g (83%) of the desired 3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]phenol product as a dark orange oil. ^{1}H NMR (acetone-d_6) δ 7.01-7.38 (m, 5H), 6.26-6.44 (m. 3H), 6.08 (t, 1H), 5.88 (tt, 1H), 4.34 (s, 2H).

[0207] **EX-20B**) A solution of 3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino] phenol (5.1 g, 16.2 mmol) from **EX-20A**, *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (1.5 mL, 17.4 mmol), and ytterbium trifluoromethanesulfonate (1.0 g, 10 mol%) in 10 mL of acetonitrile was heated at 50 °C in a sealed glass tube for 4 h. The reaction mixture was cooled to room temperature, then diluted with water and diethyl ether and extracted. The ether layer was washed with saturated aqueous sodium bicarbonate and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give 5.64 g (81%) of the desired (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy] phenyl]methyl][3,3,3-trifluoro-2-hydroxy-propyl)amino]phenol product as a yellow oil. ^{1}H NMR (acetone-d_6) δ 7.41 (t, 1H), 7.23 (d, 1H), 7.16-7.20 (m, 2H), 6.97 (t, 1H), 6.42 (tt, 1H), 6.18-6.24 (m, 3H), 4.77 (s, 2H), 4.43-4.48 (m, 1H), 3.58 (dd, 1H), 3.39 (dd, 1H).

[0208] To a solution of (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy]phenyl]methyl][3,3,3-trifluoro-2-hydroxypropyl)amino] phenol (100 mg, 0.23 mmol) from **EX-20B** and 3-trifluoromethylbenzyl bromide (70.0 mg. 0.27 mmol) in 2.5 mL of acetone was added cesium carbonate (100 mg, 0.31 mmol). The reaction mixture was heated at 60 °C for 18 h then cooled to room temperature. The reaction mixture was filtered through celite, and the filtrate was concentrated. The residue was purified by reverse phase HPLC eluting with 50% to 90% acetonitrile in water to afford 63.3 mg (45%) of the desired (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoro-methyl)phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol product as an orange oil. HRMS calcd. for $C_{26}H_{21}F_{10}NO_3$: 586.1440 $[M+H]^+$, found: 586.1419. ^{1}H NMR (acetone-d_6) δ 7.61-7.82 (m, 4H), 7.41 (t, 1H), 7.25 (d, 1H), 7.10-7.21 (m, 3H), 6.34-6.67 (m, 4H), 5.73 (d, 1H), 5.19 (s, 2H), 4.82 (s, 2H), 4.34-4.48 (m, 1H), 3.99 (dd, 1H), 3.68 (dd, 1H).

[0209] Additional examples of (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]-[3-[[aryl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanols are prepared by one skilled in the art using similar methods. as shown in, Example Table 4.

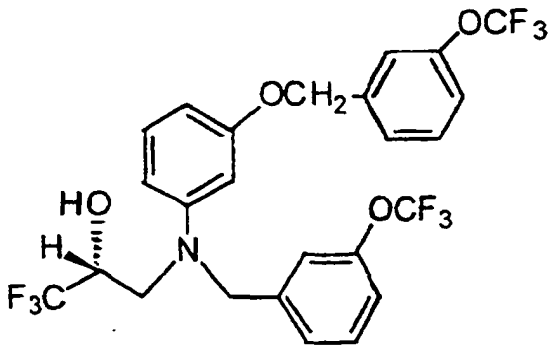
Example Table 4. (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[aryl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanols



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
21	3,5-difluorobenzyl	554.1378	554.1352
22	3-trifluoromethoxybenzyl	602.1389	602.1390
23	3-isopropyl	470.1566	464.1601

EXAMPLE 24

[0210]



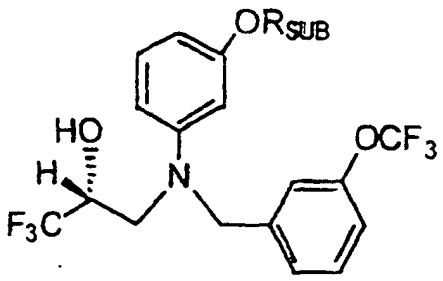
(2*R*)-3-[[3-[[3-(trifluoromethoxy)phenyl]methoxy]phenyl][[3-(trifluoromethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0211] (2*R*)-3-[[3-[[3-(trifluoromethoxy)phenyl]methoxy]phenyl][[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol can be prepared by one skilled in the art using similar methods starting from 3-(trifluoromethoxy)-benzaldehyde. HRMS calcd. for $C_{25}H_{20}F_9NO_4$: 570.1327 $[M+H]^+$, found: 570.1325. ^1H NMR (acetone-d_6) δ 7.43 (t, 1H), 7.32 (d, 1H), 7.18-7.23 (m, 2H), 7.01-7.16 (m, 3H), 6.92-7.00 (m, 1H), 6.38-6.45 (m, 3H), 5.12 (s, 2H), 4.81 (s, 2H), 4.41-4.53 (m, 1H), 3.98 (dd, 1H), 3.63 (dd, 1H).

[0212] Additional examples of (2*R*)-3-[[3-[[aryl]methoxy]phenyl][[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-tri-

fluoro-2-propanols can be prepared by one skilled in the art using similar methods, as shown in Example Table 5.

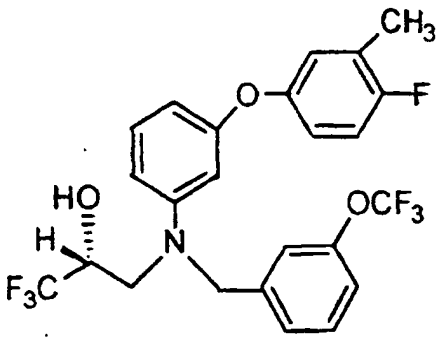
Example Table 5. (*2R*)- 3-[[3-[[aryl]methoxy]phenyl][[3-(trifluoromethoxy)-phenyl]methyl]amino]-1.1.1-trifluoro-2-propanols.



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
25	4-trifluoromethoxybenzyl	570.1327	570.1299
26	3,5-di(trifluoromethyl)benzyl	622.1252	622.1252
27	3-trifluoromethylbenzyl	554.1378	554.1369
28	3.5-difluorobenzyl	522.1315	522.1259
29	benzyl	486.1504	486.1504
30	isopropyl	438.1504	438.1509
31	cyclohexylmethyl	492.1973	492.1973
32	cyclopentyl	464.1660	464.1641

EXAMPLE 33

[0213]



(2*R*)-3-[[3-(4-fluoro-3-methylphenoxy)phenyl][[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

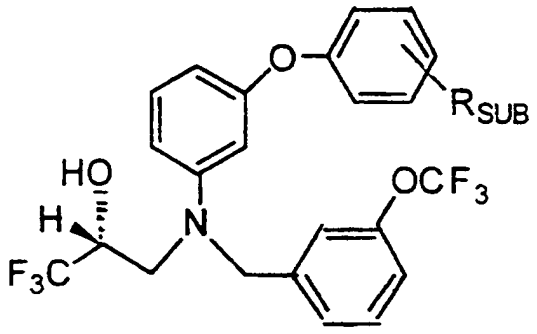
[0214] **EX-33A**) To a solution of 3-bromoaniline (5.7 mL, 52.6 mmol) and 3-trifluoromethoxybenzaldehyde (10.0 g, 52.6 mmol) in 135 mL of dichloroethane was added sodium triacetoxyborohydride (14.5 g, 68.4 mmol) and glacial acetic acid (3.1 mL, 54.7 mmol). The reaction was stirred at room temperature for 2 h, then quenched with water and extracted with dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:9 ethyl acetate in hexane to give 14.3 g (78%) of the desired of *N*-(3-bromophenyl)[[3-(trifluoromethoxy) phenyl] methyl]amine product as a dark brown oil. HRMS calcd. for $C_{14}H_{11}BrF_3NO$: 346.0055 $[M+H]^+$, found: 346.0052.

[0215] **EX-33B**) A solution of of *N*-(3-bromophenyl)[[3-(trifluoromethoxy)phenyl]methyl]-amine (10.0 g, 28.9 mmol) from **EX-33A**, *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (4.2 g, 37.6 mmol), and ytterbium (III) trifluoromethanesulfonate (1.79 g, 2.89 mmol) in 27 mL of acetonitrile was heated at 50 °C in a sealed glass tube overnight. The reaction mixture was cooled to room temperature and filtered through celite. The crude product was purified by column chromatography on silica gel eluting with 2:3 dichloromethane in hexane to afford 11.9 g (90%) of the desired (2*R*)-3-[[(3-bromophenyl)] [[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol product as a brown oil (98% ee by chiral HPLC analysis). HRMS calcd. for $C_{17}H_{14}BrF_6NO_2$: 458.0190 $[M+H]^+$, found: 458.0197.

[0216] A suspension of 4-fluoro-3-methylphenol (98.0 µL, 0.88 mmol) and cesium carbonate (319.5 mg, 0.98 mmol) in 1 mL of *N,N*-dimethylacetamide was preheated at 60 °C for 5 minutes. To this solution was added 4 mL of a stock solution containing (2*R*)-3-[[(3-bromophenyl)][[3-(trifluoromethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propanol (200 mg, 0.437 mmol) from **EX-33B,** 1-naphthoic acid (164 mg, 0.95 mmol). copper(I) trifluoromethansulfonate benzene complex (21.8 mg, 0.0434 mmol), 4 Å sieves (105 mg), and 4 mL of toluene. The reaction mixture was stirred at 105 °C for 3 weeks and 2 days. During that time, additional cesium carbonate and catalyst were added (a spatula tip of each) to the reaction three different times. The reaction was cooled to room temperature, filtered through celite, and the solvent was evaporated. The residue was purified by reverse phase HPLC eluting with 35% to 90% acetonitrile in water to afford 50.5 mg (23%) of the desired (2*R*)-3-[[3-(4-fluoro-3-methylphenoxy)phenyl][[3-(trifluoromethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propanol product as an orange oil. HRMS calcd. for $C_{24}H_{20}F_7NO_3$: 504.1410 $[M+H]^+$, found: 504.1389. ^1H NMR (acetone-d_6) δ 7.44 (t, 1H), 7.24 (d, 1H), 7.08-7.21 (m, 3H), 6.98 (t, 1H), 6.75-6.85 (m, 1H), 6.68-6.74 (m, 1H), 6.53 (d, 1H), 6.21-6.34 (m, 2H), 4.79 (t, 2H), 4.46-4.53 (m, 1H), 3.95 (dd, 1H), 2.61-2.72 (m, 1H), 2.20 (s, 3H).

[0217] Additional examples (2*R*)-3-[[(aryloxy)phenyl][[3-(trifluoromethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propanols can be prepared by one skilled in the art using similar methods, as shown in Example Table 6.

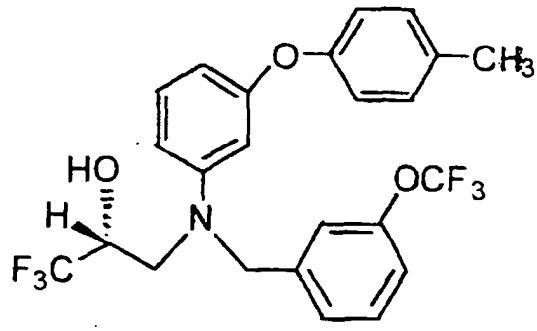
Example Table 6. (2*R*)-3-[[(aryloxy)phenyl][[3-(trifluoromethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
34	3-trifluoromethoxy	556.1170	556.1180
35	3-isopropyl	514.1817	514.1823
36	3,4-dimethyl	500.1660	500.1654
37	4-chloro-3-methyl	520.1114	520.1129
38	3-*tert*-butyl	528.1973	528.1942
39	3,4-dichloro	540.0568	540.0567
40	3,4-($CH_2CH_2CH_2CH_2$)-	526.1817	526.1788

EXAMPLE 41

[0218]



(2*R*)-3-[[3-(4-methylphenoxy)phenyl][[3-(trifluoromethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propanol

[0219] **EX-41A)** To a solution of *p*-cresol (5.76 g, 0.053 mol) and 1,3-dinitrobenzene (8.97 g, 0.053 mol) in 100 mL of dimethylsulfoxide was added cesium carbonate (43.4 g, 0.133 mol). The reaction mixture was heated at 100 °C for

18 h, then cooled to room temperature, quenched with water, and extracted with diethyl ether. The organic layers were combined, washed with 0.1 N HCl and water, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to afford 8.0 g (66%) of the desired 3-(4-methylphenoxy)nitrobenzene product as a yellow oil. ^1H NMR ($CDCl_3$) δ 7.83 (s, 1H), 7.64 (t, 1H), 7.32 (d, 1H), 7.18 (d, 1H), 7.09 (d, 2H), 6.8 (d, 2H), 2.20 (s, 1H).

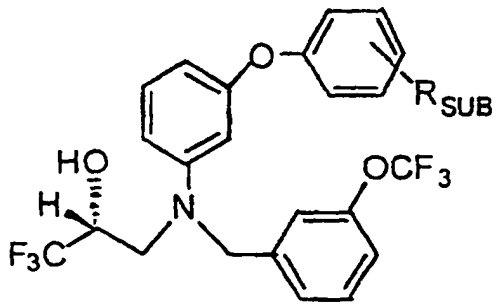
[0220] **EX-41B)** A solution of 3-(4-methylphenoxy)nitrobenzene (8.0 g, 0.035 mol) from **EX-41A** in 25 mL of ethanol under nitrogen was charged with 10% palladium on carbon (0.80 g). The resulting mixture was hydrogenated for 4 h at room temperature and 45 psi. The reaction mixture was filtered through celite and concentrated *in vacuo* to give 6.7 g (96%) of the desired 3-(4-methylphenoxy)aniline product as a yellow oil. ESMS *m/z* = 200 $[M+H]^+$ confirmed the desired $C_{13}H_{13}NO$ product and the complete consumption of starting material.

[0221] **EX-41C**) To a solution of 3-(4-methylphenoxy)aniline (2.91 g, 0.015 mol) from **EX-41B**, and 3-(trifluoromethoxy)benzyaldehyde (3.24 g, 0.015 mol) in 50 mL dichloroethane was added sodium triacetoxyborohydride (4.02 g, 0.019 mol) and glacial acetic acid (0.99 g, 0.017 mol). The reaction mixture was stirred at room temperature for 18 h, then quenched with saturated aqueous sodium bicarbonate and extracted with dichloromethane. The organic layers were combined, dried over $MgSO_4$ and concentrated *in vacuo* to give 5.38 g (91%) of the desired *N*-[3-(4-methylphenoxy)-phenyl)]-[[3-(trifluoromethoxy)phenyl]methyl]amine product as an orange oil. ESMS *m/z* = 374 $[M+H]^+$ confirmed the desired $C_{21}H_{18}NO_2F_3$ product and the complete consumption of starting material.

[0222] To a mixture of *N*-[3-(4-methylphenoxy)phenyl)]-[[3-(trifluoromethoxy)phenyl]-methyl]amine(1.3 g, 0.0035 mol) from **EX-41C** and *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.59 g, 0.0053 mol) was added a suspension of ytterbium (III) trifluoromethanesulfonate (0.22 g, 0.0004 mol) in 1.3 mL of acetonitrile. The resulting mixture was heated at 50 °C in a sealed glass tube for 18 h. The reaction mixture was cooled to room temperature, then diluted with water and extracted with ethyl acetate. The crude product was purified by column chromatography on silica gel eluting with 1:4 ethyl acetate in hexane to afford 1.03 g (61%) of the desired (2*R*)-3-[3-(4-methyl-phenoxy)phenyl)[[3-(trifluoromethoxy)phenyl] methyl]amino]-1,1,1-trifluoro-2-propa-nol product as a pure yellow oil. Anal. calcd. for $C_{24}H_{21}F_6NO_3$: C, 59.38; H, 4.36; N, 2.89. Found: C, 59.17; H, 4.62; N, 2.80. HRMS calcd.: 486.1504 $[M+H]^+$, found: 486.1513, ^1H NMR (C_6D_6) δ 6.82 (m, 8H), 6.60 (dd, 1H), 6.42 (dd, 1H), 6.38 (s, 1H),. 6.18 (dd, 1H), 4.00 (s, 2H), 3.63 (m, 1H), 3.40 (d, 1H), 3.02 (m, 1H), 2.00 (s, 3H), 1.40 (d, 1H). ^{19}F NMR (C_6D_6) δ -57.98 (s, 3F), -78.50 (s. 3F).

[0223] Additional examples of (2*R*)-3-[3-(substituted-phenoxy)phenyl]-[[3-(trifluoro-methoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanols can prepared by one skilled in the art using similar methods. as shown in Example Table 7.

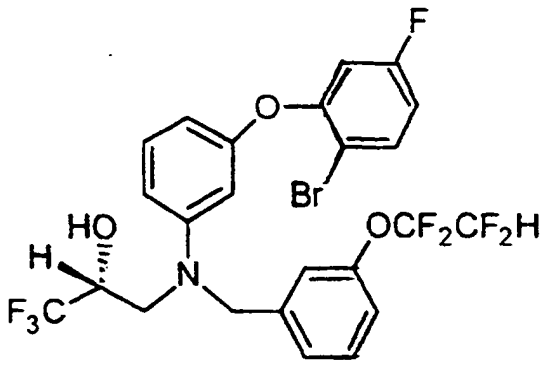
Example Table 7. (2*R*)- 3-[3-(substituted-phenoxy)phenyl][[3-(trifluoromethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
42	4-fluoro	490.1253	490.1238

EXAMPLE 43

[0224]



(2*R*)-3-[[3-(2-bromo-5-fluorophenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

[0225] **EX-43A**) To a solution of 3-aminophenol (5 g, 46 mmol), 1-bromo-2,4-difluorobenzene (10 g, 50 mmol) and Cs_2CO_3 (16 g, 50 mmol) in 25 mL of dimethylformamide was added solid $(CuOTf)_2C_6H_6$ (100 mg), and the mixture was stirred under nitrogen at 85 °C for 22 h, at which time HPLC analysis indicated that the reaction had gone to completion and formed two products. The DMF was removed under reduced pressure. The residue was diluted with ether and filtered through a celite pad. The pad was washed with ether and a small amount of water. The mixture was extracted with ether several times. The combined ether layers were washed with water and brine, then dried over $MgSO_4$. The dried organic layer was evaporated to give 10.2 g (80%) of the desired product, which consisted of a 11:1 ratio of 3-(2-bromo-5-fluoro-phenoxy)aniline and 3-(4-bromo-3-fluorophenoxy)aniline. The crude product was purified by flash column chromatography on silica gel eluting with 1:7:0.01 of ethyl acetate:hexane:ammonium hydroxide to give 8.8 g (68%) of the desired product as a yellow oil, which was a 25:1 ratio of 3-(2-bromo-5-fluorophenoxy)aniline and 3-(4-bromo-3-fluorophenoxy)aniline. HRMS calcd. for $C_{12}H_9NOFBr$: 281.9930 $[M+H]^+$, found: 281.9950.

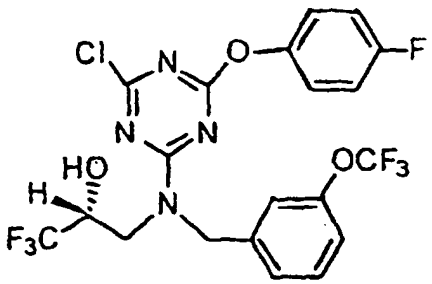
[0226] **EX-43B**) The 3-(2-bromo-5-fluorophenoxy)aniline (1.39 g, 4.95 mmol) product from **EX-43A** and 3-(1,1,2,2-tetrafluoroethoxy)benzaldehyde (1.0 g, 4.5 mmol) were dissolved in 15 mL of dichloroethane and acetic acid (0.30 mL, 5.4 mmol), then solid $NaBH(OAc)_3$ (1.26 g, 5.9 mmol) was added. The mixture was stirred at room temperature for 1 h, then quenched with water and extracted with ether. The ether layer was washed with water and brine, then dried over $MgSO_4$, and evaporated to give 2.1 g (97%) of crude product, which was purified by flash column chromatography on silica gel eluting with 1:7:0.01 of ethyl acetate:hexane:ammonium hydroxide to give 2.0 g (91%) of the desired 3-[3-(2-bromo-5-fluoro-phenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amine product. as a light yellow oil, > 90% pure by HPLC analysis. HRMS calcd. for $C_{21}H_{15}NO_2BrF_5$: 488.0285 $[M+H]^+$, found: 488.0269.

[0227] The 3-[3-(2-bromo-5-fluorophenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]-methyl]amine (0.5 g, 2.0 mmol) product from **EX-43B** and *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.17 g, 2.0 mmol) from **EX-4** were dissolved in 0.5 mL of acetonitrile. Ytterbium (III) trifluoromethanesulfonate (0.06 g, 0.1 mmol) was added, and the stirred solution was warmed to 40 °C for 1 h, at which time HPLC analysis indicated that no secondary amine starting material remained. The reaction was quenched with water and extracted with ether. The ether layer was washed with water and brine. then dried over $MgSO_4$. The crude product was purified by flash column chromatography on silica gel eluting with 1:7:0.01 of ethyl acetate:hexane:ammonium hydroxide to give 0.4 g (67%) of the desired *R*-(+)-3-[[3-(2-bromo-5-fluorophenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol product as a light yellow oil (> 84% ee by chiral HPLC analysis). Anal. calcd. for $C_{24}H_{18}BrF_8NO_3$: C, 48.02; H, 3.02; N, 2.33. found: C, 48.07; H, 3.14: N. 2.31. HRMS calcd.: 600.0420 $[M+H]^+$, found: 600.0386. ^1H NMR ($CDCl_3$) δ 7.5 0 (dd, 1H), 7.30 (t, 1H), 7.18 (t, 1H), 7.07 (t, 2H), 6.99 (s, 1H), 6.70 (dt, 1H), 6.56 (dd, 1H), 6.52 (dd, 1H), 6.38 (dd, 1H), 6.32 (m, 1H), 5.87 (tt, 1H,), 4.65 (d, 2H). 4.33 (m, 1H), 3.85 (dd, 1H), 3.56 (dd, 1H), 2.48 (bs, 1H). NOE difference spectra confirmed that the isolated material was the indicated *N*-[3-(2-bromo-5-fluorophenoxy)phenyl]-3-aminopropanol product. ^{19}F NMR ($CDCl_3$) δ -79.24 (d, 3F), -88.57 (m, 2F), -112.04 (q, 1H), -137.16 (dt, 2F).

EXAMPLE 44

(Included for reference and/or comparison only)

[0228]



(2*R*)-*N*-[2-chloro-6-(p-fluorophenoxy)-1,3,5-triazin-4-yl]-3-[[[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol

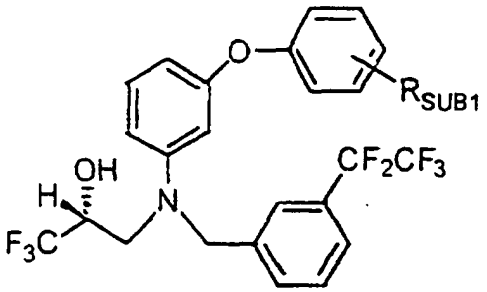
[0229] **EX-44A)** 3-Trifluoromethoxybenzenemethanamine (1.15g, 6 mmol) and *R*-(+)-1,1,1-trifluoro-2,3-epoxypropane (0.67 g, 6 mmol) were combined and stirred at 80 °C for 1.5 h. The mixture was cooled to room temperature, and the resulting solid was recrystallized from hot hexanes. The white solid was isolated by vacuum filtration and washed with cold hexanes to give 0.67 g (37%) of pure (2*R*)-3-[[[3-(trifluoro-methoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol. ^{1}H NMR ($CDCl_3$) δ 7.37 (t, 1H), 7.24 (d, 1H), 7.15 (m, 2H), 3.99 (m, 1H), 3.85 (d, 2H), 2.98 (dd, 1H), 2.88 (dd, 1H), 2.79 (s, 1H). ^{19}F NMR ($CDCl_3$) δ - 58.19 (s, 3F), -78.88 (s, 3F). HRMS calcd, for $C_{11}H_{11}F_6NO_2$: 304.0772 $[M+H]^+$, found: 304.0794.

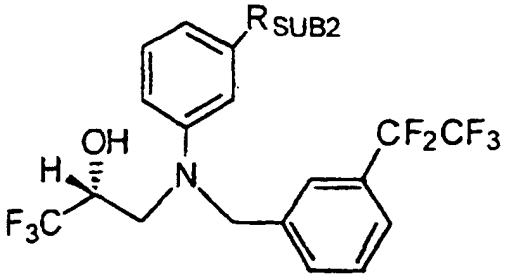
[0230] **EX-44B**) To a solution of p-fluorophenol 1.00 g (8.92 mmol) in 30 mL of tetrahydrofuran at 0 °C was added a 60% dispersion of sodium hydride in mineral oil (0.36 g, 8.92 mmol). After 30 min, cyanuric chloride (1.64 g, 8.92 mmol) was added as a heterogeneous mixture in tetrahydrofuran at 0 °C. The reaction mixture was allowed to slowly warm to room temperature. After 14 h, the mixture was cooled to 0 °C. and a saturated aqueous NH_4Cl solution was added. The aqueous solution was extracted with diethyl ether (3 x 50 mL). The combined ether extracts were washed with brine. dried ($MgSO_4$), and concentrated *in vacuo* to afford 1.34 g (58%) of the desired 2.4-dichloro-6-(4-fluorophenoxy)-1,3,5-triazine product as an off white solid which was taken on to the next step without purification. MS *m/z* = 260 $[M+H]^+$.

[0231] To a stirred solution of aminopropanol from **EX-44A** (0.100 g, 0.330 mmol) in *N,N*-dimethylformamide at 0 °C was added the 2,4-dichloro-(4-fluorophenoxy)-1,3,5-triazine ether product from **EX-44B** (0.086 g, 0.330 mmol) as a solution in *N,N*-di-methylformamide. The reaction mixture was allowed to slowly warm to room temperature. After 14 h, the reaction mixture was cooled to 0 °C, and a saturated aq. $NaHCO_3$ solution was added. After stirring the reaction mixture for 30 min at room temperature, the aqueous layer was extracted with ether (3 x 30 mL). The combined ether extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give a yellow oil. The crude residue was purified by column chromatography on silica gel eluting with 20 % ethyl acetate in hexanes to give 0.075 g (43%) of the desired (2*R*)-*N*-[2-chloro-6-(p-fluorophenoxy)-1,3,5-triazin-4-yl]-3-[[[3-(trifluoromethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol product as a pale yellow oil. HRMS calcd. for $C_{20}H_{14}ClF_7N_4O_3$: 526.0643 $[M^+]$, found: 526.0632. ^{1}H NMR (C_6D_6) δ 6.95 (s, 1H), 6.63 (m, 14H), 4.74 (d, 1H), 4.37 (d, 1H), 4.16 (d, 1H), 4.00 (d, 2H), 3.73 (m, 1H), 3.48 (m, 2H), 3.26 (m, 2H), 3.12 (m, 2H).

[0232] Based on the preceding procedures, additional substituted (2*R*)-3-[(*N*-aryl)-[[aryl]methyl]amino]-1,1,1-trifluoro-2-propanols are prepared by one skilled in the art using similar methods, as shown in Example Table 8. Substituted (3*R*)-4-[*N*-(aryl)-[(aryl)methyl]amino]-1,1,1,2,2-pentafluoro-3-butanols are prepared by one skilled in the art using similar methods, as shown in Example Table 9. Substituted (2*R*)-3-[*N*-(aryl)[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanois are prepared by one skilled in the art using similar methods, as shown in Example Table 10. Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl]amino]-1,1-difluoro-1-chloro-2-propanols are prepared by one skilled in the art using similar methods, as shown in Example Table 11. Substituted (2*R*)-3-[*N,N*-(diaryl)amino]-1,1,1-trifluoro-2-propanols are prepared by one skilled in the art using similar methods. as shown in Example Table 12.

Example Table 8. Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl]amino]-1,1,1-trifluoro-2-propanols.





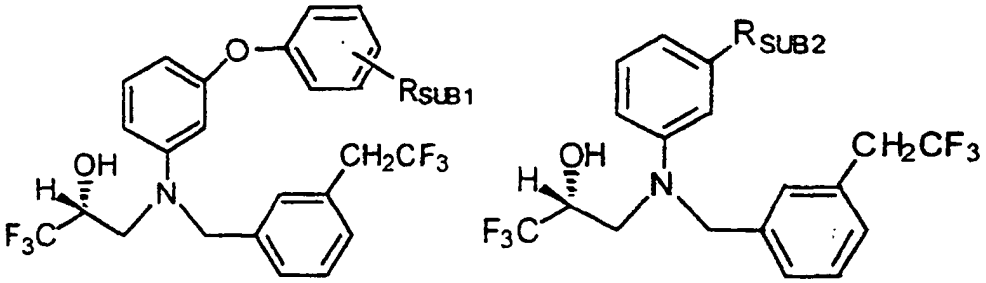
Ex. No.	R_{SUB1}
45	3-isopropyl
46	2-Cl, 3-Cl
47	3-CF_3O
48	4-F
49	4-CH_3
50	2-F, 5-Br
51	3-CF_3CF_2
52	3-CH_3CH_2
53	3-CH_3, 5-CH_3
54	3-$(CH_3)_3C$
55	4-F, 3-CH_3
56	3-Cl, 4-Cl
57	3,4-$(CH_2)_4$
58	3-HCF_2CF_2O
59	3-CHF_2O
60	3-$(CH_3)_2N$
61	3-cyclopropyl
62	3-(2-furyl)
63	3-CF_3CF_2
64	4-NH_2
65	3-CH_3, 4-CH_3, 5-CH_3

Ex. No.	R_{SUB2}
69	3-CF_3O-benzyloxy
70	3-CF_3-benzyloxy
71	3-F, 5-F-benzyloxy
72	cyclohexylmethyleneoxy
73	benzyloxy
74	3-CF_3, 5-CF_3-benzyloxy
75	4-CF_3O-benzyloxy
76	4-CH_3CH_2-benzyloxy
77	isopropoxy
78	3-CF_3-benzyl
79	isopropylthio
80	cyclopentoxy
81	3-Cl-5-pyridinyloxy
82	3-CF_3S-benzyloxy
83	3-CH_3, 4-CH_3-benzyloxy
84	2-F, 3-CF_3-benzyloxy
85	3-F, 5-CF_3-benzyloxy
86	4-$(CH_3)_2CH$-benzyloxy
87	1-phenylethoxy
88	4-F, 3-CH_3-benzoyl
89	3-CF_3-phenyl

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
66	4-$CH_3CH_2CH_2O$
67	3-CF_3
68	2-NO_2

Ex. No.	R_{SUB2}
90	4-CH_3O-phenylamino
91	cyclopropoxy
92	4-NO_2-phenylthio



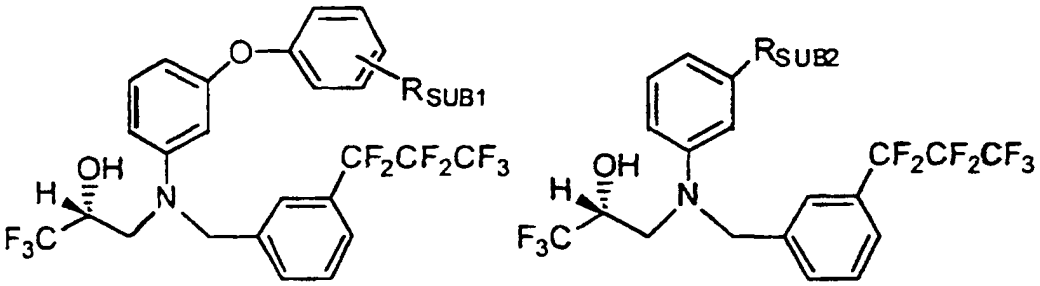
Ex. No.	R_{SUB1}
93	3-isopropyl
94	2-Cl, 3-Cl
95	3-CF_3O
96	4-F
97	4-CH_3
98	2-F, 5-Br
99	4-Cl, 3-CH_3CH_2
100	3-CH_3CH_2
101	3-CH_3, 5-CH_3
102	3-$(CH_3)_3C$
103	4-F, 3-CH_3
104	3-Cl, 4-Cl
105	3,4-$(CH_2)_4$
106	3-HCF_2CF_2O
107	3-CHF_2O

Ex. No.	R_{SUB2}
117	3-CF_3O-benzyloxy
118	3-CF_3-benzyloxy
119	3-F, 5-F-benzyloxy
120	cyclohexylmethyleneoxy
121	benzyloxy
122	3-CF_3, 5-CF_3-benzyloxy
123	4-CF_3O-benzyloxy
124	4-CH_3CH_2-benzyloxy
125	isopropoxy
126	3-CF_3-benzyl
127	isopropylthio
128	cyclopentoxy
129	3-Cl-5-pyridinyloxy
130	3-CF_3S-benzyloxy
131	3-CH_3, 4-CH_3-benzyloxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
108	3-$(CH_3)_2N$
109	3-cyclopropyl
110	3-(2-furyl)
111	3-CF_3CF_2
112	4-NH_2
113	3-CH_3, 4-CH_3, 5-CH_3
114	4-$CH_3CH_2CH_2O$
115	3-CF_3
116	2-NO_2

Ex. No.	R_{SUB2}
132	2-F, 3-CF_3-benzyloxy
133	3-F, 5-CF_3-benzyloxy
134	4-$(CH_3)_2CH$-benzyloxy
135	1-phenylethoxy
136	4-F, 3-CH_3-benzoyl
137	3-CF_3-phenyl
138	4-CH_3O-phenylamino
139	cyclopropoxy
140	4-NO_2-phenylthio



Ex. No.	R_{SUB1}
141	3-isopropyl
142	2-Cl, 3-Cl
143	3-CF_3O
144	4-F
145	4-CH_3
146	2-F, 5-Br
147	4-Cl, 3-CH_3CH_2
148	3-CH_3CH_2

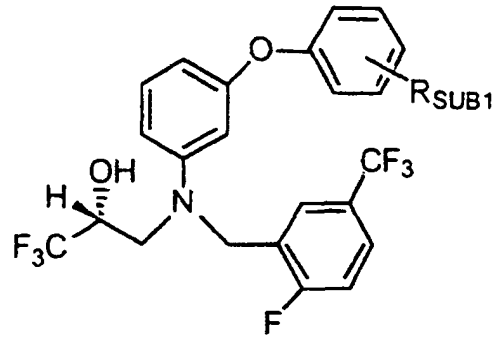
Ex. No.	R_{SUB2}
165	3-CF_3O-benzyloxy
166	3-CF_3-benzyloxy
167	3-F, 5-F-benzyloxy
168	cyclohexylmethyleneoxy
169	benzyloxy
170	3-CF_3, 5-CF_3-benzyloxy
171	4-CF_3O-benzyloxy
172	4-CH_3CH_2-benzyloxy

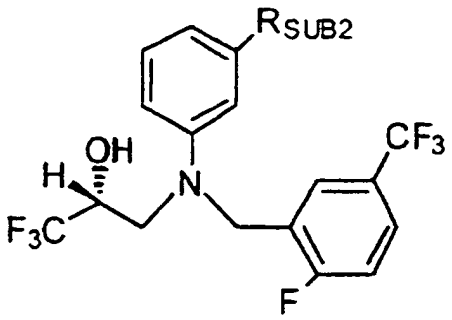
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
149	3-CH_3, 5-CH_3
150	3-$(CH_3)_3C$
151	4-F, 3-CH_3
152	3-Cl, 4-Cl
153	3,4-$(CH_2)_4$
154	3-HCF_2CF_2O
155	3-CHF_2O
156	3-$(CH_3)_2N$
157	3-cyclopropyl
158	3-(2-furyl)
159	3-CF_3CF_2
160	4-NH_2
161	3-CH_3, 4-CH_3, 5-CH_3
162	4-$CH_3CH_2CH_2O$
163	3-CF_3
164	2-NO_2

Ex. No.	R_{SUB2}
173	isopropoxy
174	3-CF_3-benzyl
175	isopropylthio
176	cyclopentoxy
177	3-Cl-5-pyridinyloxy
178	3-CF_3S-benzyloxy
179	3-CH_3, 4-CH_3-benzyloxy
180	2-F, 3-CF_3-benzyloxy
181	3-F, 5-CF_3-benzyloxy
182	4-$(CH_3)_2CH$-benzyloxy
183	1-phenylethoxy
184	4-F, 3-CH_3-benzoyl
185	3-CF_3-phenyl
186	4-CH_3O-phenylamino
187	cyclopropoxy
188	4-NO_2-phenylthio

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.





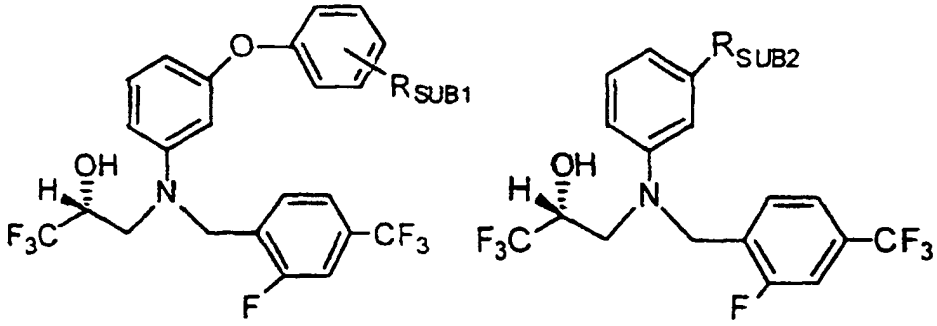
Ex. No.	R_{SUB1}
189	3-isopropyl
190	2-Cl, 3-Cl
191	3-CF_3O
192	4-F
193	4-CH_3
194	2-F, 5-Br
195	4-Cl, 3-CH_3
196	3-CH_3CH_2
197	3-CH_3, 5-CH_3
198	3-$(CH_3)_3C$
199	4-F, 3-CH_3
200	3-Cl, 4-Cl
201	3,4-$(CH_2)_4$
202	3-HCF_2CF_2O
203	3-CHF_2O
204	3-$(CH_3)_2N$
205	3-cyclopropyl
206	3-(2-furyl)
207	3-CF_3CF_2

Ex. No.	R_{SUB2}
213	3-CF_3O-benzyloxy
214	3-CF_3-benzyloxy
215	3-F, 5-F-benzyloxy
216	cyclohexylmethyleneoxy
217	benzyloxy
218	3-CF_3, 5-CF_3-benzyloxy
219	4-CF_3O-benzyloxy
220	4-CH_3CH_2-benzyloxy
221	isopropoxy
222	3-CF_3-benzyl
223	isopropylthio
224	cyclopentoxy
225	3-Cl-5-pyridinyloxy
226	3-CF_3S-benzyloxy
227	3-CH_3, 4-CH_3-benzyloxy
228	2-F, 3-CF_3-benzyloxy
229	3-F, 5-CF_3-benzyloxy
230	4-$(CH_3)_2CH$-benzyloxy
231	1-phenylethoxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
208	4-NH_2
209	3-CH_3, 4-CH_3, 5-CH_3
210	4-$CH_3CH_2CH_2O$
211	3-CF_3
212	2-NO_2

Ex. No.	R_{SUB2}
232	4-F, 3-CH_3-benzoyl
233	3-CF_3-phenyl
234	4-CH_3O-phenylamino
235	cyclopropoxy
236	4-NO_2-phenylthio



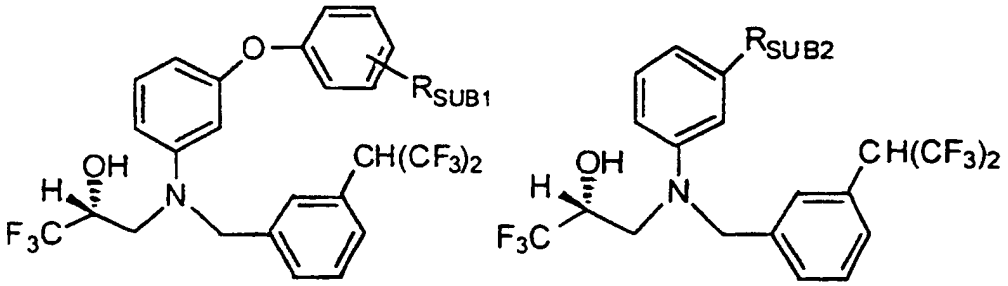
Ex. No.	R_{SUB1}
237	3-isopropyl
238	2-Cl, 3-Cl
239	3-CF_3O
240	4-F
241	4-CH_3
242	2-F, 5-Br
243	4-Cl, 3-CH_3
244	3-CH_3CH_2
245	3-CH_3, 5-CH_3
246	3-$(CH_3)_3C$
247	4-F, 3-CH_3
248	3-Cl, 4-Cl

Ex. No.	R_{SUB2}
261	3-CF_3O-benzyloxy
262	3-CF_3-benzyloxy
263	3-F, 5-F-benzyloxy
264	cyclohexylmethyleneoxy
265	benzyloxy
266	3-CF_3, 5-CF_3-benzyloxy
267	4-CF_3O-benzyloxy
268	4-CH_3CH_2-benzyloxy
269	isopropoxy
270	3-CF_3-benzyl
271	isopropylthio
272	cyclopentoxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
249	3,4-$(CH_2)_4$
250	3-HCF_2CF_2O
251	3-CHF_2O
252	3-$(CH_3)_2N$
253	3-cyclopropyl
254	3-(2-furyl)
255	3-CF_3CF_2
256	4-NH_2
257	3-CH_3, 4-CH_3, 5-CH_3
258	4-$CH_3CH_2CH_2O$
259	3-CF_3
260	2-NO_2

Ex. No.	R_{SUB2}
273	3-Cl-5-pyridinyloxy
274	3-CF_3S-benzyloxy
275	3-CH_3, 4-CH_3-benzyloxy
276	2-F, 3-CF_3-benzyloxy
277	3-F, 5-CF_3-benzyloxy
278	4-$(CH_3)_2CH$-benzyloxy
279	1-phenylethoxy
280	4-F, 3-CH_3-benzoyl
281	3-CF_3-phenyl
282	4-CH_3O-phenylamino
283	cyclopropoxy
284	4-NO_2-phenylthio



Ex. No.	R_{SUB1}
285	3-isopropyl
286	2-Cl, 3-Cl
287	3-CF_3O
288	4-F
289	4-CH_3

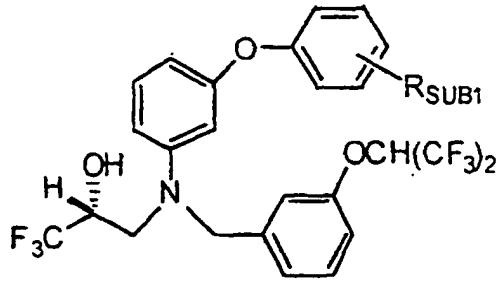
Ex. No.	R_{SUB2}
309	3-CF_3O-benzyloxy
310	3-CF_3-benzyloxy
311	3-F, 5-F-benzyloxy
312	cyclohexylmethyleneoxy
313	benzyloxy

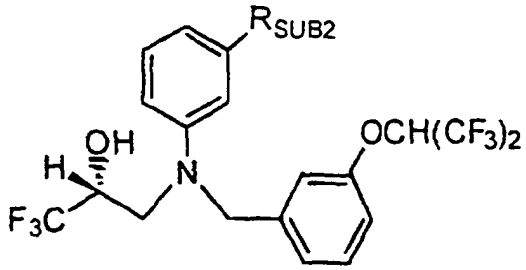
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
290	2-F, 5-Br
291	4-Cl, 3-CH_3CH_2
292	3-CH_3CH_2
293	3-CH_3, 5-CH_3
294	3-$(CH_3)_3C$
295	4-F, 3-CH_3
296	3-Cl, 4-Cl
297	3,4-$(CH_2)_4$
298	3-HCF_2CF_2O
299	3-CHF_2O
300	3-$(CH_3)_2N$
301	3-cyclopropyl
302	3-(2-furyl)
303	3-CF_3CF_2
304	4-NH_2
305	3-CH_3, 4-CH_3, 5-CH_3
306	4-$CH_3CH_2CH_2O$
307	3-CF_3
308	2-NO_2

Ex. No.	R_{SUB2}
314	3-CF_3, 5-CF_3-benzyloxy
315	4-CF_3O-benzyloxy
316	4-CH_3CH_2-benzyloxy
317	isopropoxy
318	3-CF_3-benzyl
319	isopropylthio
320	cyclopentoxy
321	3-Cl-5-pyridinyloxy
322	3-CF_3S-benzyloxy
323	3-CH_3, 4-CH_3-benzyloxy
324	2-F, 3-CF_3-benzyloxy
325	3-F, 5-CF_3-benzyloxy
326	4-$(CH_3)_2CH$-benzyloxy
327	1-phenylethoxy
328	4-F, 3-CH_3-benzoyl
329	3-CF_3-phenyl
330	4-CH_3O-phenylamino
331	cyclopropoxy
332	4-NO_2-phenylthio

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.





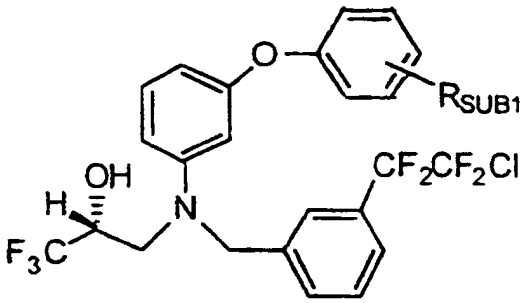
Ex. No.	R_{SUB1}
333	3-isopropyl
334	2-Cl, 3-Cl
335	3-CF_3O
336	4-F
337	4-CH_3
338	2-F, 5-Br
339	4-Cl, 3-CH_3CH_2
340	3-CH_3CH_2
341	3-CH_3, 5-CH_3
342	3-$(CH_3)_3C$
343	4-F, 3-CH_3
344	3-Cl, 4-Cl
345	3,4-$(CH_2)_4$
346	3-HCF_2CF_2O
347	3-CHF_2O
348	3-$(CH_3)_2N$
349	3-cyclopropyl
350	3-(2-furyl)
351	3-CF_3CF_2
352	4-NH_2

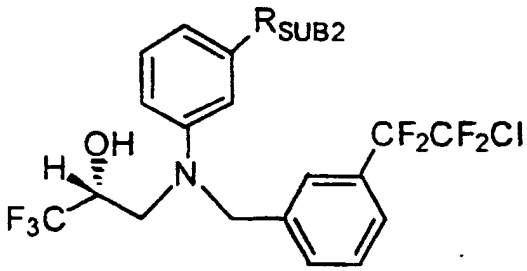
Ex. No.	R_{SUB2}
357	3-CF_3O-benzyloxy
358	3-CF_3-benzyloxy
359	3-F, 5-F-benzyloxy
360	cyclohexylmethyleneoxy
361	benzyloxy
362	3-CF_3, 5-CF_3-benzyloxy
363	4-CF_3O-benzyloxy
364	4-CH_3CH_2-benzyloxy
365	isopropoxy
366	3-CF_3-benzyl
367	isopropylthio
368	cyclopentoxy
369	3-Cl-5-pyridinyloxy
370	3-CF_3S-benzyloxy
371	3-CH_3, 4-CH_3-benzyloxy
372	2-F, 3-CF_3-benzyloxy
373	3-F, 5-CF_3-benzyloxy
374	4-$(CH_3)_2CH$-benzyloxy
375	1-phenylethoxy
376	4-F, 3-CH_3-benzoyl

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
353	3-CH_3, 4-CH_3, 5-CH_3
354	4-$CH_3CH_2CH_2O$
355	3-CF_3
356	2-NO_2

Ex. No.	R_{SUB2}
377	3-CF_3-phenyl
378	4-CH_3O-phenylamino
379	cyclopropoxy
380	4-NO_2-phenylthio





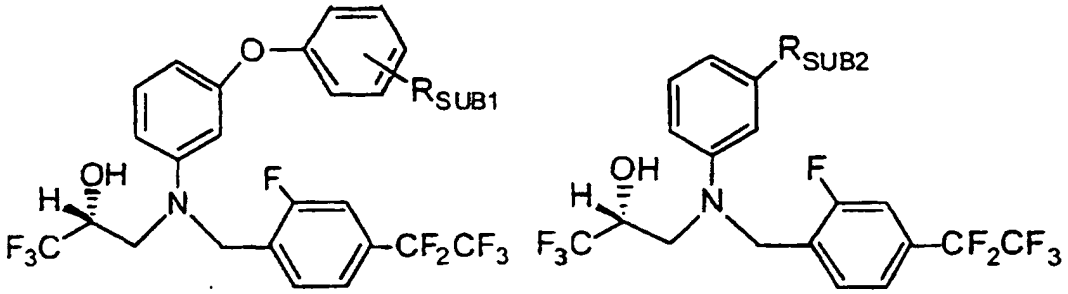
Ex. No.	R_{SUB1}
381	3-isopropyl
382	2-Cl, 3-Cl
383	3-CF_3O
384	4-F
385	4-CH_3
386	2-F, 5-Br
387	4-Cl, 3-CH_3CH_2
388	3-CH_3CH_2
389	3-CH_3, 5-CH_3
390	3-$(CH_3)_3C$
391	4-F, 3-CH_3
392	3-Cl, 4-Cl
393	3,4-$(CH_2)_4$

Ex. No.	R_{SUB2}
405	3-CF_3O-benzyloxy
406	3-CF_3-benzyloxy
407	3-F, 5-F-benzyloxy
408	cyclohexylmethyleneoxy
409	benzyloxy
410	3-CF_3, 5-CF_3-benzyloxy
411	4-CF_3O-benzyloxy
412	4-CH_3CH_2-benzyloxy
413	isopropoxy
414	3-CF_3-benzyl
415	isopropylthio
416	cyclopentoxy
417	3-Cl-5-pyridinyloxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
394	3-HCF_2CF_2O
395	3-CHF_2O
396	3-$(CH_3)_2N$
397	3-cyclopropyl
398	3-(2-furyl)
399	3-CF_3CF_2
400	4-NH_2
401	3-CH_3, 4-CH_3, 5-CH_3
402	4-$CH_3CH_2CH_2O$
403	3-CF_3
404	2-NO_2

Ex. No.	R_{SUB2}
418	3-CF_3S-benzyloxy
419	3-CH_3, 4-CH_3-benzyloxy
420	2-F, 3-CF_3-benzyloxy
421	3-F, 5-CF_3-benzyloxy
422	4-$(CH_3)_2CH$-benzyloxy
423	1-phenylethoxy
424	4-F, 3-CH_3-benzoyl
425	3-CF_3-phenyl
426	4-CH_3O-phenylamino
427	cyclopropoxy
428	4-NO_2-phenylthio



Ex. No.	R_{SUB1}
429	3-isopropyl
430	2-Cl, 3-Cl
431	3-CF_3O
432	4-F
433	4-CH_3
434	2-F, 5-Br

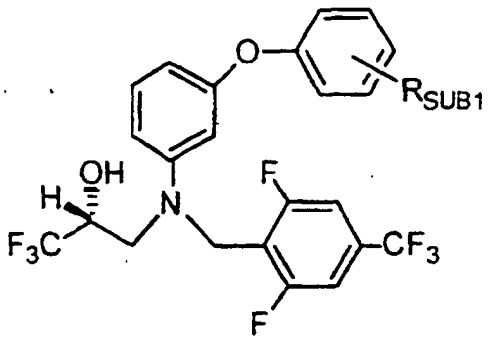
Ex. No.	R_{SUB2}
453	3-CF_3O-benzyloxy
454	3-CF_3-benzyloxy
455	3-F, 5-F-benzyloxy
456	cyclohexylmethyleneoxy
457	benzyloxy
458	3-CF_3, 5-CF_3-benzyloxy

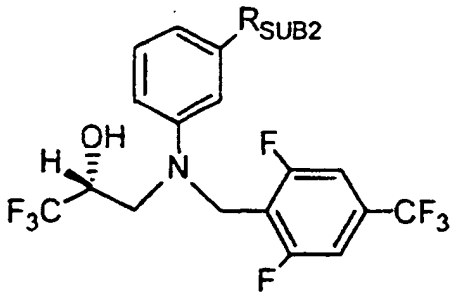
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
435	4-Cl, 3-CH_3CH_2
436	3-CH_3CH_2
437	3-CH_3, 5-CH_3
438	3-$(CH_3)_3C$
439	4-F, 3-CH_3
440	3-Cl, 4-Cl
441	3,4-$(CH_2)_4$
442	3-HCF_2CF_2O
443	3-CHF_2O
444	3-$(CH_3)_2N$
445	3-cyclopropyl
446	3-(2-furyl)
447	3-CF_3CF_2
448	4-NH_2
449	3-CH_3, 4-CH_3, 5-CH_3
450	4-$CH_3CH_2CH_2O$
451	3-CF_3
452	2-NO_2

Ex. No.	R_{SUB2}
459	4-CF_3O-benzyloxy
460	4-CH_3CH_2-benzyloxy
461	isopropoxy
462	3-CF_3-benzyl
463	isopropylthio
464	cyclopentoxy
465	3-Cl-5-pyridinyloxy
466	3-CF_3S-benzyloxy
467	3-CH_3, 4-CH_3-benzyloxy
468	2-F, 3-CF_3-benzyloxy
469	3-F, 5-CF_3-benzyloxy
470	4-$(CH_3)_2CH$-benzyloxy
471	1-phenylethoxy
472	4-F, 3-CH_3-benzoyl
473	3-CF_3-phenyl
474	4-CH_3O-phenylamino
475	cyclopropoxy
476	4-NO_2-phenylthio

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.





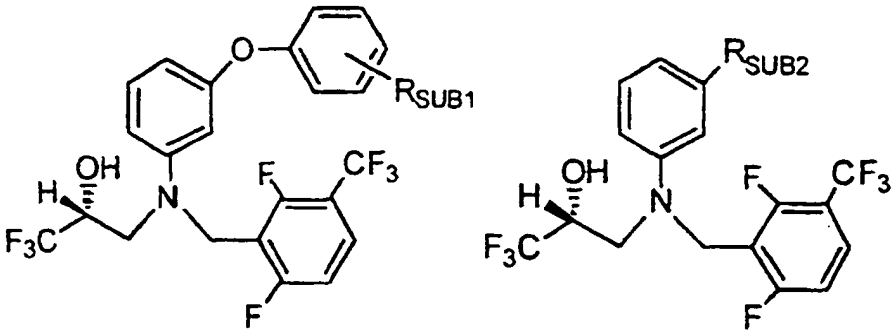
Ex. No.	R_{SUB1}
477	3-isopropyl
478	2-Cl, 3-Cl
479	3-CF_3O
480	4-F
481	4-CH_3
482	2-F, 5-Br
483	4-Cl, 3-CH_3CH_2
484	3-CH_3CH_2
485	3-CH_3, 5-CH_3
486	3-$(CH_3)_3C$
487	4-F, 3-CH_3
488	3-Cl, 4-Cl
489	3,4-$(CH_2)_4$
490	3-HCF_2CF_2O
491	3-CHF_2O
492	3-$(CH_3)_2N$
493	3-cyclopropyl
494	3-(2-furyl)
495	3-CF_3CF_2

Ex. No.	R_{SUB2}
501	3-CF_3O-benzyloxy
502	3-CF_3-benzyloxy
503	3-F, 5-F-benzyloxy
504	cyclohexylmethyleneoxy
505	benzyloxy
506	3-CF_3, 5-CF_3-benzyloxy
507	4-CF_3O-benzyloxy
508	4-CH_3CH_2-benzyloxy
509	isopropoxy
510	3-CF_3-benzyl
511	isopropylthio
512	cyclopentoxy
513	3-Cl-5-pyridinyloxy
514	3-CF_3S-benzyloxy
515	3-CH_3, 4-CH_3-benzyloxy
516	2-F, 3-CF_3-benzyloxy
517	3-F, 5-CF_3-benzyloxy
518	4-$(CH_3)_2CH$-benzyloxy
519	1-phenylethoxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
496	4-NH_2
497	3-CH_3, 4-CH_3, 5-CH_3
498	4-$CH_3CH_2CH_2O$
499	3-CF_3
500	2-NO_2

Ex. No.	R_{SUB2}
520	4-F, 3-CH_3-benzoyl
521	3-CF_3-phenyl
522	4-CH_3O-phenylamino
523	cyclopropoxy
524	4-NO_2-phenylthio



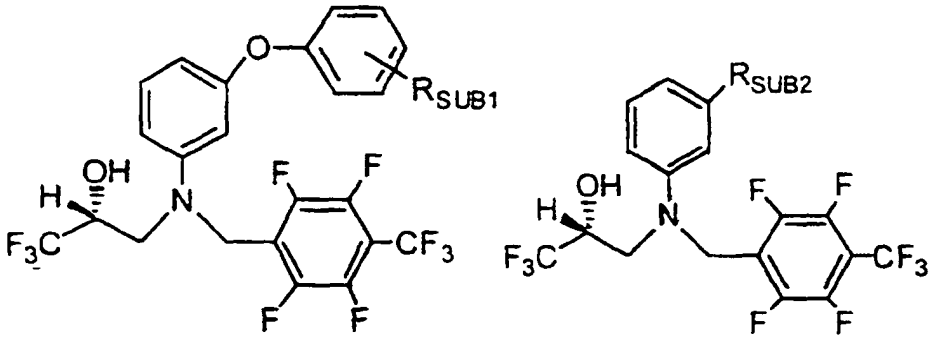
Ex. No.	R_{SUB1}
525	3-isopropyl
526	2-Cl, 3-Cl
527	3-CF_3O
528	4-F
529	4-CH_3
530	2-F, 5-Br
531	4-Cl, 3-CH_3CH_2
532	3-CH_3CH_2
533	3-CH_3, 5-CH_3
534	3-$(CH_3)_3C$
535	4-F, 3-CH_3
536	3-Cl, 4-Cl

Ex. No.	R_{SUB2}
549	3-CF_3O-benzyloxy
550	3-CF_3-benzyloxy
551	3-F, 5-F-benzyloxy
552	cyclohexylmethyleneoxy
553	benzyloxy
554	3-CF_3, 5-CF_3-benzyloxy
555	4-CF_3O-benzyloxy
556	4-CH_3CH_2-benzyloxy
557	isopropoxy
558	3-CF_3-benzyl
559	isopropylthio
560	cyclopentoxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
537	3,4-$(CH_2)_4$
538	3-HCF_2CF_2O
539	3-CHF_2O
540	3-$(CH_3)_2N$
541	3-cyclopropyl
542	3-(2-furyl)
543	3-CF_3CF_2
544	4-NH_2
545	3-CH_3, 4-CH_3, 5-CH_3
546	4-$CH_3CH_2CH_2O$
547	3-CF_3
548	2-NO_2

Ex. No.	R_{SUB2}
561	3-Cl-5-pyridinyloxy
562	3-CF_3S-benzyloxy
563	3-CH_3, 4-CH_3-benzyloxy
564	2-F, 3-CF_3-benzyloxy
565	3-F, 5-CF_3-benzyloxy
566	4-$(CH_3)_2CH$-benzyloxy
567	1-phenylethoxy
568	4-F, 3-CH_3-benzoyl
569	3-CF_3-phenyl
570	4-CH_3O-phenylamino
571	cyclopropoxy
572	4-NO_2-phenylthio



Ex. No.	R_{SUB1}
573	3-isopropyl
574	2-Cl, 3-Cl
575	3-CF_3O
576	4-F

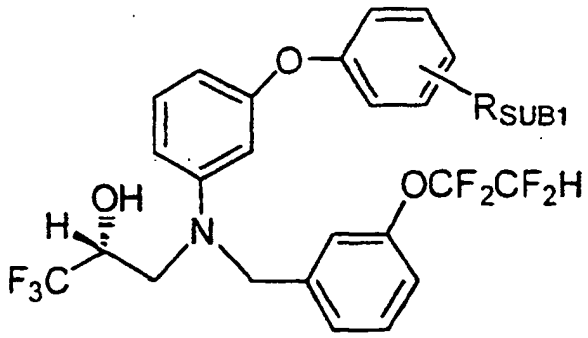
Ex. No.	R_{SUB2}
597	3-CF_3O-benzyloxy
598	3-CF_3-benzyloxy
599	3-F, 5-F-benzyloxy
600	cyclohexylmethyleneoxy

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
577	4-CH_3
578	2-F, 5-Br
579	4-Cl, 3-CH_3CH_2
580	3-CH_3CH_2
581	3-CH_3, 5-CH_3
582	3-$(CH_3)_3C$
583	4-F, 3-CH_3
584	3-Cl, 4-Cl
585	3,4-$(CH_2)_4$
586	3-HCF_2CF_2O
587	3-CHF_2O
588	3-$(CH_3)_2N$
589	3-cyclopropyl
590	3-(2-furyl)
591	3-CF_3CF_2
592	4-NH_2
593	3-CH_3, 4-CH_3, 5-CH_3
594	4-$CH_3CH_2CH_2O$
595	3-CF_3
596	2-NO_2

Ex. No.	R_{SUB2}
601	benzyloxy
602	3-CF_3, 5-CF_3-benzyloxy
603	4-CF_3O-benzyloxy
604	4-CH_3CH_2-benzyloxy
605	isopropoxy
606	3-CF_3-benzyl
607	isopropylthio
608	cyclopentoxy
609	3-Cl-5-pyridinyloxy
610	3-CF_3S-benzyloxy
611	3-CH_3, 4-CH_3-benzyloxy
612	2-F, 3-CF_3-benzyloxy
613	3-F, 5-CF_3-benzyloxy
614	4-$(CH_3)_2CH$-benzyloxy
615	1-phenylethoxy
616	4-F, 3-CH_3-benzoyl
617	3-CF_3-phenyl
618	4-CH_3O-phenylamino
619	cyclopropoxy
620	4-NO_2-phenylthio

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB1}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
621	4-F	522.1315	522.1297
622	2-Cl, 3-Cl	572.0630	572.0653
623	2-F, 5-Br	600.0420	600.0404
624	4-Cl, 3-CH_3	551.1098	551.1101
625	3-CH_3, 5-CH_3	532.1722	532.1705
626	3-$(CH_3)_3C$	560.2035	560.2055
627	4-F, 3-CH_3	536.1471	536.1480
628	3-Cl, 4-Cl	572.0630	572.0630
629	3,4-$(CH_2)_4$	558.1879	558.1881
630	3-HCF_2CF_2O		
631	3-CHF_2O		
632	3-$(CH_3)_2N$	547.1831	547.1844
633	3-cyclopropyl		
634	3-(2-furyl)		
635	3-CF_3CF_2		
636	3-cyclopentyl		
637	4-NH_2	519.1519	519.1529

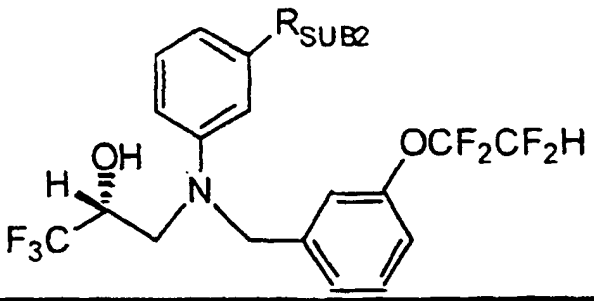
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
638	3-CH_3, 4-CH_3, 5-CH_3	546.1879	546.1901
639	4-CH_3CH_2O	547.1594	547.1594
640	3-CF_3		
641	2-NO_2	549.1260	549.1235
642	3,4-dimethyl	531.1644	531.1649
643	3-methyl, 5-ethyl	546.1879	546.1899
644	3-methyl	517.1488	517.1493
645	2,3-difluoro	540.1221	540.1182
646	4-CF_3	572.1282	572.1268
647	2-fluoro, 3-CF_3	590.1189	590.1184
648	2-fluoro, 4-CF_3	590.1189	590.1155
649	2-chloro, 4-fluoro	556.0925	556.0891
650	4-*n*-propyl	546.1879	546.1878
651	3-chloro, 4-fluoro	556.0925	556.0932
652	2,4-difluoro	540.1221	540.1194
653	3,5-difluoro	540.1221	540.1217
654	3,4-difluoro	540.1221	540.1248
655	3-fluoro	522.1315	522.1337
656	2-chloro	538.1019	538.1021
657	2-fluoro	522.1315	522.1310
658	2,5-difluoro	540.1221	540.1255
659	4-chloro, 2-fluoro	556.0926	556.0954
660	2,4-dichloro	572.0630	572.0667
661	2-fluoro, 3-CH_3		
662	4-chloro	537.0942	537.0944

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
663	4-isopropyl. 3-methyl	560.2035	560.2035
664	2,3,4-trifluoro	558.1127	558.1161
665	2,3,5-trifluoro	558.1127	558.1109
666	4-propoxy	562.1828	562.1803
667	4-isopropyl	546.1879	546.1899
668	4-CF_3O-	588.1233	588.1241
669	4-butoxy	576.1958	576.1969
670	3-methyl. 4-CH_3S-	564.1443	564.1476
671	4-nitro	549.1260	549.1306
672	3-CF_3S-		
673	4-chloro. 3-fluoro	556.0925	556.0933
674	3,5-dimethoxy	564.1623	564.1617
675	4-bromo	582.0716	582.0473
676	4-*sec*-butyl	560.2035	560.2051
677	3-fluoro-2-nitro	567.1166	567.1135
678	3-methoxy	533.1437	533.1450
679	4-bromo-2-nitro	627.0366	627.0375
680	4-cyano	529.1362	529.1364
681	4-CH_3S-	550.1209	550.1251
682	3,4-$(CH=CH)_2$	554.1566	554.1578
683	4-CH_3CH_2NH-	547.1832	547.1819
684	4-propionyl	560.1672	560.1694
685	3-phenyl	580.1723	580.1772
686	4-cyclopentyl	572.2035	572.2029

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
687	6-methyl-3-pyridinyloxy	518.1440	518.1452
688	5-chloro-3-pyridinyloxy	539.0972	539.1002
689	3-pyridinyloxy	505.1362	505.1369
690	2-methyl-3-pyridinyloxy	519.1518	519.1517
691	5-indolinyloxy	543.1519	543.1630
692	4-fluoro-2-pyridinyloxy	523.1268	523.1243
693	2-cyano-3-pyridinyloxy	530.1315	530.1300
694	5-bromo-2-pyridinyloxy	583.0667	583.0405
695	3-CF_3-2-pyridinyloxy	573.1236	573.1205
696	2-pyridinylmethyleneoxy	519.1519	519.1522
697	cyclohexylmethyleneoxy	524.2036	524.2028
698	isopropoxy	470.1488	470.1565
699	cyclopentyloxy	496.1723	496.1719
700	*neo*-pentoxy	498.1879	498.1845
701	4-(methoxycarbonyl)-butoxy	542.1777	542.1827
702	trifluoromethoxy	496.0971	496.0959
703	2-methylpropoxy	484.1723	484.1718
704	2-methoxyethoxy	486.1515	486.1537
705	2-oxobutoxy	498.1515	498.1529
706	cyclohexyloxy	510.1880	510.1910

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
707	(methoxycarbonyl)methoxy	500.1308	500.1297
708	4-tetrahydropyranyloxy	512.1672	512.1631
709	1-phenylethoxy	532.1723	532.1711
710	3-CF_3O-benzyloxy	602.1389	602.1380
711	3-trifluoromethyl-benzyloxy	586.1440	586.1419
712	3,5-dimethyl-benzyloxy	546.1879	546.1890
713	3-bromo-benzyloxy	596.0671	596.0641
714	3-CF_3S-benzyloxy	618.1161	618.1151
715	3,4-dimethyl-benzyloxy	546.1879	546.1881
716	3,5-difluoro-benzyloxy	554.1378	554.1390
717	2-fluoro-3-CF_3-benzyloxy	604.1346	604.1329
718	benzyloxy	518.1566	518.1578
719	3,5-$(CF_3)_2$-benzyloxy	654.1314	654.1308
720	3-fluoro-5-CF_3-benzyloxy	604.1346	604.1309
721	4-CF_3O-benzyloxy	602.1389	602.1383
722	3-chloro-benzyloxy	552.1176	552.1157
723	4-ethyl-benzyloxy	546.1879	546.1862
724	3-methyl-benzyloxy	532.1723	532.1692
725	2-fluoro-benzyloxy	536.1472	536.1465
726	2,3-difluoro-benzyloxy	554.1378	554.1364
727	4-isopropyl-benzyloxy	560.2036	560.2020
728	4-methyl-benzyloxy	532.1723	532.1729
729	4-bromo-benzyloxy	596.0671	596.0669
730	4-CF_3-benzyloxy	586.1440	586.1400
731	4-fluoro-benzyloxy	536.1472	536.1454

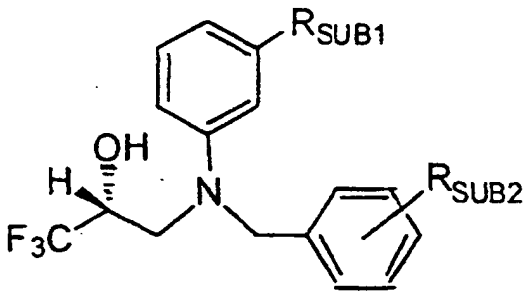
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
732	3-iodo-benzyloxy	644.0533	644.0517
733	4-CF_3S-benzyloxy	618.1161	618.1165
734	4-CF_2HO-benzyloxy	584.1483	584.1480
735	4-fluoro-3-CF_3-benzyloxy	604.1346	604.1336
736	2,3,5-trifluoro-benzyloxy	572.1284	572.1276
737	4-chloro-benzyloxy	552.1176	552.1188
738	2,5-difluoro-benzyloxy	554.1378	554.1350
739	3-chloro-2-fluoro-benzyloxy	570.1082	570.1069
740	2,4-$(CF_3)_2$-benzyloxy	654.1314	654.1321
741	3,5-dichloro-benzyloxy	586.1787	586.1378
742	3-methoxy-benzyloxy	548.1672	548.1676
743	4-cyano-benzyloxy	543.1519	543.1517
744	4-*tert*-butyl-benzyloxy	574.2192	574.2163
745	isopropylthio	486.1338	486.1351
746	4-nitrophenylthio	565.1032	565.1034
747	4-acetylphenylthio	562.1287	562.1261
748	(4-chloro-thien-2-yl)-methylthio	574.0512	574.0523
749	4-methoxy-phenylamino	532.1597	532.1592
750	3-methoxy-phenylamino	532.1597	532.1593
751	4-chloro-phenylamino	536.1102	536.1125
752	4-*n*-propyl-phenylamino	544.1961	544.1959
753	3-cyano-phenylamino	527.1444	527.1448
754	3-CF_3-benzyl	570.1413	570.1480
755	3-methyl-4-fluoro-benzyl	534.1679	534.1688
756	3-CF_3-phenyl	556.1334	556.1339

Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.

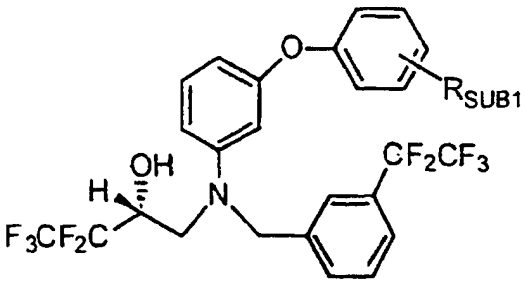
Ex. No.	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
757	2,4-dichloro-phenyl	556.0681	556.0651
758	3-methoxybenzyl	532.1723	532.1705
759	4-methoxyphenyl	518.1566	518.1533
760	3-chloro-4-fluoro-phenyl	540.0976	540.0957
761	4-fluoro-3-methyl-benzoyl	548.1410	548.1441
762	3-chlorobenzyl	536.1227	536.1218
763	3,4-dimethylbenzyl	530.1930	530.1887
764	3,5-dichlorobenzyl	570.0838	570.0801
765	2,3,4-trifluorophenyl	542.1177	542.1152
766	3-chloro-4-fluoro-benzyl	554.1133	554.1108
767	4-fluoro-3-methyl-phenyl	520.1523	520.1494
768	3-methyl-4-chloro-benzyl	550.1384	550.1380
769	2-methylpropanoyl	482.1566	482.1576
770	4-methylthiobenzyl	548.1494	548.1503
771	4-fluorophenyl	506.1366	506.1336
772	4-chlorophenyl	522.1071	522.1049
773	3-methoxyphenyl	518.1566	518.1544
774	4-methylbenzyl	516.1774	516.1769
775	1-hydroxy-2-methyl-propyl	484.1723	484.1725
776	benzyl	502.1617	502.1609
777	2-CF_3-phenyl	556.1334	556.1286
778	3,4-dichlorophenyl	556.0681	556.0698
779	benzoyl	516.1410	516.1383
780	4-fluorobenzoyl	534.1315	534.1273
781	N-piperidinyl	494.1804	494.1804
782	phenyl	488.1460	488.1457
783	thien-2-yl	494.1024	494.0987

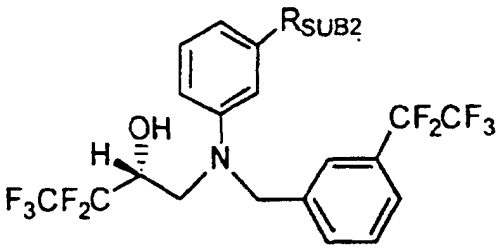
Example Table 8 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)methyl] amino]-1,1,1-trifluoro-2-propanols.



Ex. No.	R_{SUB1}	R_{SUB2}	Calculated Mass $[M+H]^+$	Observed Mass $[M+H]^+$
784	phenoxy	3-cyclopentyl	456.2150	456.2143
785	phenoxy	3-isopropoxy	446.1943	446.1936
786	phenoxy	3-CF_3S	488.1119	488.1116
787	4-F-phenoxy	3-CF_3S	505.0946	505.0927
788	4-F-phenoxy	3-*sec*-butoxy	478.2005	478.1880
789	phenoxy	3-$(CF_3)_2COH$-	554.1378	554.1385
790	4-CH_3-phenoxy	3-CF_3S	502.1275	502.1261
791	phenoxy	3-(2-furyl)	454.1630	454.1635
792	4-F-phenoxy	3-isopropoxy	464.1849	464.1867
793	phenoxy	3-isobutyl	444.2150	444.2157
794	phenoxy	3-*tert*-butoxy	460.2100	460.2103
795	4-F-phenoxy	3-CH_3CH_2O-	450.1692	450.1682
796	4-F-phenoxy	3-CF_3O-	490.1253	490.1211
797	phenoxy	4-F-3-(2-furyl)-	472.1536	472.1530
798	4-F-phenoxy	3-*n*-propoxy-	464.1849	464.1820
799	4-F-phenoxy	3-cyclopentyloxy-	490.2005	490.1998
800	phenoxy	3-(3-furyl)-	454.1630	454.1646
801	4-F-phenoxy	3-cyclopropyl-methyleneoxy	476.1849	476.1857
802	phenoxy	3-CF_3CH_2O-	486.1504	486.1498

Example Table 9. (3*R*)-4-[*N*-(aryl)-[(aryl)methyl]amino]-1,1,1,2,2-pentafluoro-3-butanols.





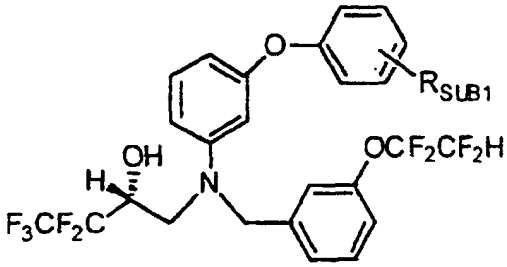
Ex. No.	R_{SUB1}
803	3-isopropyl
804	2-Cl, 3-Cl
805	3-CF_3O
806	4-F
807	4-CH_3
808	2-F, 5-Br
809	4-Cl, 3-CH_3CH_2
810	3-CH_3CH_2
811	3-CH_3, 5-CH_3
812	3-$(CH_3)_3C$
813	4-F, 3-CH_3
814	3-Cl, 4-Cl
815	3,4-$(CH_2)_4$
816	3-HCF_2CF_2O
817	3-CHF_2O
818	3-$(CH_3)_2N$
819	3-cyclopropyl
820	3-(2-furyl)
821	3-CF_3CF_2
822	4-NH_2
823	3-CH_3, 4-CH_3, 5-CH_3
824	4-$CH_3CH_2CH_2O$

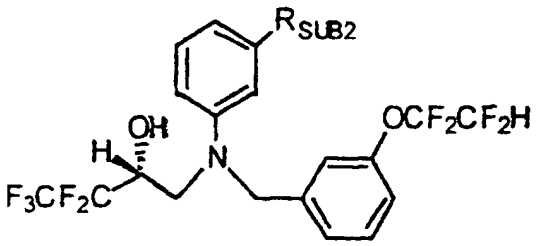
Ex. No.	R_{SUB2}
827	3-CF_3O-benzyloxy
828	3-CF_3-benzyloxy
829	3-F, 5-F-benzyloxy
830	cyclohexylmethyleneoxy
831	benzyloxy
832	3-CF_3, 5-CF_3-benzyloxy
833	4-CF_3O-benzyloxy
834	4-CH_3CH_2-benzyloxy
835	isopropoxy
836	3-CF_3-benzyl
837	isopropylthio
838	cyclopentoxy
839	3-Cl-5-pyridinyloxy
840	3-CF_3S-benzyloxy
841	3-CH_3, 4-CH_3-benzyloxy
842	2-F, 3-CF_3-benzyloxy
843	3-F, 5-CF_3-benzyloxy
844	4-$(CH_3)_2CH$-benzyloxy
845	1-phenylethoxy
846	4-F, 3-CH_3-benzoyl
847	3-CF_3-phenyl
848	4-CH_3O-phenylamino

Example Table 9. (3*R*)-4-[*N*-(aryl)-[(aryl)methyl]amino]-1,1,1,2,2-pentafluoro-3-butanols (Continued).

Ex. No.	R_{SUB1}
825	3-CF_3
826	2-NO_2

Ex. No.	R_{SUB2}
849	cyclopropoxy
850	4-NO_2-phenylthio





Ex. No.	R_{SUB1}
851	3-isopropyl
852	2-Cl, 3-Cl
853	3-CF_3O
854	4-F
855	4-CH_3
856	2-F, 5-Br
857	4-Cl, 3-CH_3CH_2
858	3-CH_3CH_2
859	3-CH_3, 5-CH_3
860	3-$(CH_3)_3C$
861	4-F, 3-CH_3
862	3-Cl, 4-Cl
863	3,4-$(CH_2)_4$
864	3-HCF_2CF_2O
865	3-CHF_2O
866	3-$(CH_3)_2N$
867	3-cyclopropyl
868	3-(2-furyl)

Ex. No.	R_{SUB2}
875	3-CF_3O-benzyloxy
876	3-CF_3-benzyloxy
877	3-F, 5-F-benzyloxy
878	cyclohexylmethyleneoxy
879	benzyloxy
880	3-CF_3, 5-CF_3-benzyloxy
881	4-CF_3O-benzyloxy
882	4-CH_3CH_2-benzyloxy
883	isopropoxy
884	3-CF_3-benzyl
885	isopropylthio
886	cyclopentoxy
887	3-Cl-5-pyridinyloxy
888	3-CF_3S-benzyloxy
889	3-CH_3, 4-CH_3-benzyloxy
890	2-F, 3-CF_3-benzyloxy
891	3-F, 5-CF_3-benzyloxy
892	4-$(CH_3)_2CH$-benzyloxy

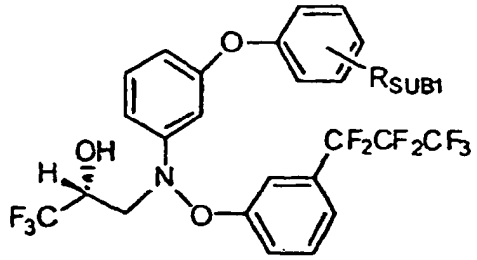
Example Table 9. (3*R*)-4-[*N*-(aryl)-[(aryl)methyl]amino]-1,1,1,2,2-pentafluoro-3-butanols (Continued).

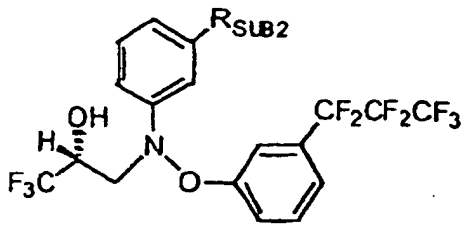
Ex. No.	R_{SUB1}
869	3-CF_3CF_2
870	4-NH_2
871	3-CH_3, 4-CH_3, 5-CH_3
872	4-$CH_3CH_2CH_2O$
873	3-CF_3
874	2-NO_2

Ex. No.	R_{SUB2}
893	1-phenylethoxy
894	4-F, 3-CH_3-benzoyl
895	3-CF_3-phenyl
896	4-CH_3O-phenylamino
897	cyclopropoxy
898	4-NO_2-phenylthio

Example Table 10. Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

(Included for reference and/or comparison only)





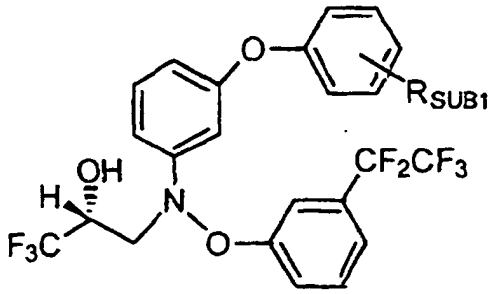
Ex. No.	R_{SUB1}
899	3-isopropyl
900	2-Cl, 3-Cl
901	3-CF_3O
902	4-F
903	4-CH_3
904	2-F, 5-Br
905	4-Cl, 3-CH_3CH_2
906	3-CH_3CH_2
907	3-CH_3, 5-CH_3
908	3-$(CH_3)_3C$
909	4-F, 3-CH_3
910	3-Cl, 4-Cl
911	3,4-$(CH_2)_4$
912	3-HCF_2CF_2O
913	3-CHF_2O
914	3-$(CH_3)_2N$
915	3-cyclopropyl
916	3-(2-furyl)
917	3-CF_3CF_2
918	4-NH_2
919	3-CH_3, 4-CH_3, 5-CH_3
920	4-$CH_3CH_2CH_2O$
921	3-CF_3

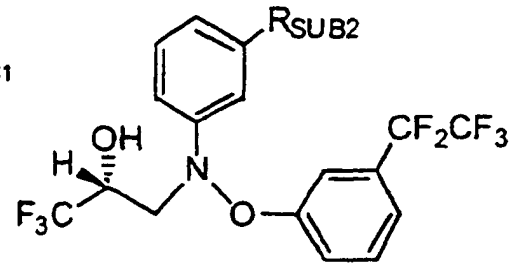
Ex. No.	R_{SUB2}
923	3-CF_3O-benzyloxy
924	3-CF_3-benzyloxy
925	3-F, 5-F-benzyloxy
926	cyclohexylmethyleneoxy
927	benzyloxy
928	3-CF_3, 5-CF_3-benzyloxy
929	4-CF_3O-benzyloxy
930	4-CH_3CH_2-benzyloxy
931	isopropoxy
932	3-CF_3-benzyl
933	isopropylthio
934	cyclopentoxy
935	3-Cl-5-pyridinyloxy
936	3-CF_3S-benzyloxy
937	3-CH_3, 4-CH_3-benzyloxy
938	2-F, 3-CF_3-benzyloxy
939	3-F, 5-CF_3-benzyloxy
940	4-$(CH_3)_2CH$-benzyloxy
941	1-phenylethoxy
942	4-F, 3-CH_3-benzoyl
943	3-CF_3-phenyl
944	4-CH_3O-phenylamino
945	cyclopropoxy

Example Table 10 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
922	2-NO_2

Ex. No.	R_{SUB2}
946	4-NO_2-phenylthio





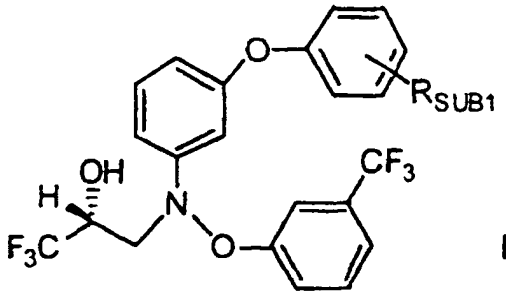
Ex. No.	R_{SUB1}
947	3-isopropyl
948	2-Cl, 3-Cl
949	3-CF_3O
950	4-F
951	4-CH_3
952	2-F, 5-Br
953	4-Cl, 3-CH_3CH_2
954	3-CH_3CH_2
955	3-CH_3, 5-CH_3
956	3-$(CH_3)_3C$
957	4-F, 3-CH_3
958	3-Cl, 4-Cl
959	3,4-$(CH_2)_4$
960	3-HCF_2CF_2O
961	3-CHF_2O
962	3-$(CH_3)_2N$
963	3-cyclopropyl
964	3-(2-furyl)

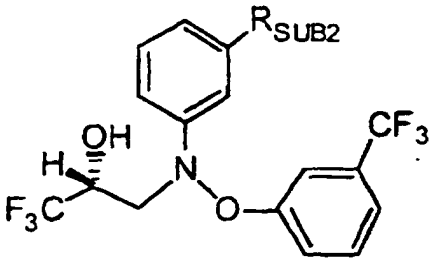
Ex. No.	R_{SUB2}
971	3-CF_3O-benzyloxy
972	3-CF_3-benzyloxy
973	3-F, 5-F-benzyloxy
974	cyclohexylmethyleneoxy
975	benzyloxy
976	3-CF_3, 5-CF_3-benzyloxy
977	4-CF_3O-benzyloxy
978	4-CH_3CH_2-benzyloxy
979	isopropoxy
980	3-CF_3-benzyl
981	isopropylthio
982	cyclopentoxy
983	3-Cl-5-pyridinyloxy
984	3-CF_3S-benzyloxy
985	3-CH_3, 4-CH_3-benzyloxy
986	2-F, 3-CF_3-benzyloxy
987	3-F, 5-CF_3-benzyloxy
988	4-$(CH_3)_2CH$-benzyloxy

Example Table 10 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
965	3-CF_3CF_2
966	4-NH_2
967	3-CH_3, 4-CH_3, 5-CH_3
968	4-$CH_3CH_2CH_2O$
969	3-CF_3
970	2-NO_2

Ex. No.	R_{SUB2}
989	1-phenylethoxy
990	4-F, 3-CH_3-benzoyl
991	3-CF_3-phenyl
992	4-CH_3O-phenylamino
993	cyclopropoxy
994	4-NO_2-phenylthio





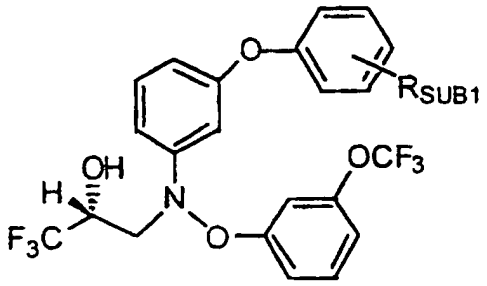
Ex. No.	R_{SUB1}
995	3-isopropyl
996	2-Cl, 3-Cl
997	3-CF_3O
998	4-F
999	4-CH_3
1000	2-F, 5-Br
1001	4-Cl, 3-CH_3CH_2
1002	3-CH_3CH_2
1003	3-CH_3, 5-CH_3
1004	3-$(CH_3)_3C$
1005	4-F, 3-CH_3
1006	3-Cl, 4-Cl
1007	3,4-$(CH_2)_4$

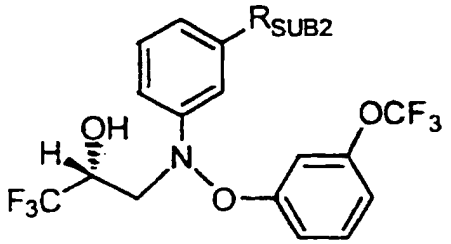
Ex. No.	R_{SUB2}
1019	3-CF_3O-benzyloxy
1020	3-CF_3-benzyloxy
1021	3-F, 5-F-benzyloxy
1022	cyclohexylmethyleneoxy
1023	benzyloxy
1024	3-CF_3, 5-CF_3-benzyloxy
1025	4-CF_3O-benzyloxy
1026	4-CH_3CH_2-benzyloxy
1027	isopropoxy
1028	3-CF_3-benzyl
1029	isopropylthio
1030	cyclopentoxy
1031	3-Cl-5-pyridinyloxy

Example Table 10 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1008	3-HCF_2CF_2O
1009	3-CHF_2O
1010	3-$(CH_3)_2N$
1011	3-cyclopropyl
1012	3-(2-furyl)
1013	3-CF_3CF_2
1014	4-NH_2
1015	3-CH_3, 4-CH_3, 5-CH_3
1016	4-$CH_3CH_2CH_2O$
1017	3-CF_3
1018	2-NO_2

Ex. No.	R_{SUB2}
1032	3-CF_3S-benzyloxy
1033	3-CH_3, 4-CH_3-benzyloxy
1034	2-F, 3-CF_3-benzyloxy
1035	3-F, 5-CF_3-benzyloxy
1036	4-$(CH_3)_2CH$-benzyloxy
1037	1-phenylethoxy
1038	4-F, 3-CH_3-benzoyl
1039	3-CF_3-phenyl
1040	4-CH_3O-phenylamino
1041	cyclopropoxy
1042	4-NO_2-phenylthio





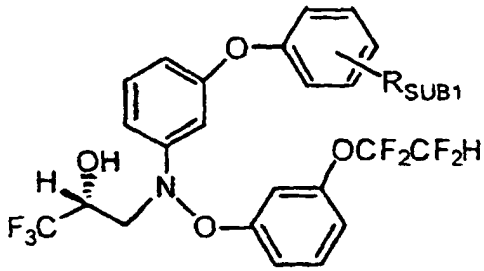
Ex. No.	R_{SUB1}
1043	3-isopropyl
1044	2-Cl, 3-Cl
1045	3-CF_3O
1046	4-F
1047	4-CH_3
1048	2-F, 5-Br
1049	4-Cl, 3-CH_3CH_2
1050	3-CH_3CH_2

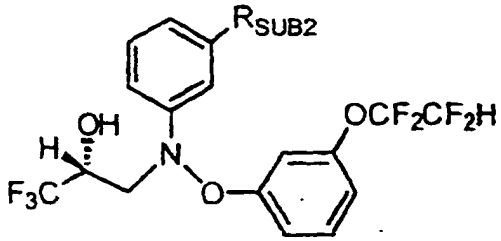
Ex. No.	R_{SUB2}
1067	3-CF_3O-benzyloxy
1068	3-CF_3-benzyloxy
1069	3-F, 5-F-benzyloxy
1070	cyclohexylmethyleneoxy
1071	benzyloxy
1072	3-CF_3, 5-CF_3-benzyloxy
1073	4-CF_3O-benzyloxy
1074	4-CH_3CH_2-benzyloxy

Example Table 10 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1051	3-CH_3, 5-CH_3
1052	3-$(CH_3)_3C$
1053	4-F, 3-CH_3
1054	3-Cl, 4-Cl
1055	3,4-$(CH_2)_4$
1056	3-HCF_2CF_2O
1057	3-CHF_2O
1058	3-$(CH_3)_2N$
1059	3-cyclopropyl
1060	3-(2-furyl)
1061	3-CF_3CF_2
1062	4-NH_2
1063	3-CH_3, 4-CH_3, 5-CH_3
1064	4-$CH_3CH_2CH_2O$
1065	3-CF_3
1066	2-NO_2

Ex. No.	R_{SUB2}
1075	isopropoxy
1076	3-CF_3-benzyl
1077	isopropylthio
1078	cyclopentoxy
1079	3-Cl-5-pyridinyloxy
1080	3-CF_3S-benzyloxy
1081	3-CH_3, 4-CH_3-benzyloxy
1082	2-F, 3-CF_3-benzyloxy
1083	3-F, 5-CF_3-benzyloxy
1084	4-$(CH_3)_2CH$-benzyloxy
1085	1-phenylethoxy
1086	4-F, 3-CH_3-benzoyl
1087	3-CF_3-phenyl
1088	4-CH_3O-phenylamino
1089	cyclopropoxy
1090	4-NO_2-phenylthio





Ex. No.	R_{SUB1}
1091	3-isopropyl
1092	2-Cl, 3-Cl
1093	3-CF_3O
1094	4-F

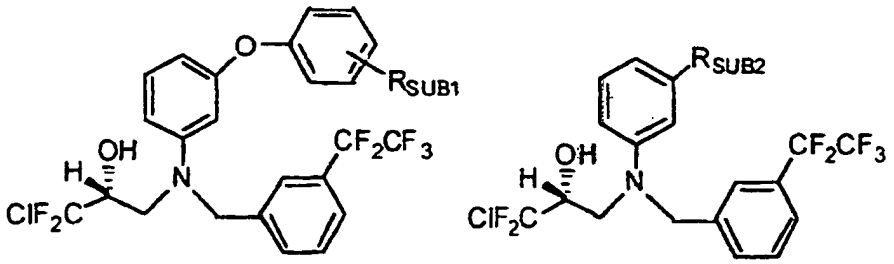
Ex. No.	R_{SUB2}
1115	3-CF_3O-benzyloxy
1116	3-CF_3-benzyloxy
1117	3-F, 5-F-benzyloxy
1118	cyclohexylmethyleneoxy

Example Table 10 (continued). Substituted (2*R*)-3-[*N*-(aryl)-[(aryl)oxy]amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1095	4-CH_3
1096	2-F, 5-Br
1097	4-Cl, 3-CH_3CH_2
1098	3-CH_3CH_2
1099	3-CH_3, 5-CH_3
1100	3-$(CH_3)_3C$
1101	4-F, 3-CH_3
1102	3-Cl, 4-Cl
1103	3,4-$(CH_2)_4$
1104	3-HCF_2CF_2O
1105	3-CHF_2O
1106	3-$(CH_3)_2N$
1107	3-cyclopropyl
1108	3-(2-furyl)
1109	3-CF_3CF_2
1110	4-NH_2
1111	3-CH_3, 4-CH_3, 5-CH_3
1112	4-$CH_3CH_2CH_2O$
1113	3-CF_3
1114	2-NO_2

Ex. No.	R_{SUB2}
1119	benzyloxy
1120	3-CF_3, 5-CF_3-benzyloxy
1121	4-CF_3O-benzyloxy
1122	4-CH_3CH_2-benzyloxy
1123	isopropoxy
1124	3-CF_3-benzyl
1125	isopropylthio
1126	cyclopentoxy
1127	3-Cl-5-pyridinyloxy
1128	3-CF_3S-benzyloxy
1129	3-CH_3, 4-CH_3-benzyloxy
1130	2-F, 3-CF_3-benzyloxy
1131	3-F, 5-CF_3-benzyloxy
1132	4-$(CH_3)_2CH$-benzyloxy
1133	1-phenylethoxy
1134	4-F, 3-CH_3-benzoyl
1135	3-CF_3-phenyl
1136	4-CH_3O-phenylamino
1137	cyclopropoxy
1138	4-NO_2-phenylthio

Example Table 11. (2*R*)-3-[*N*-(aryl)-[(aryl)methyl]amino]-1,1-difluoro-1-chloro-2-propanols.



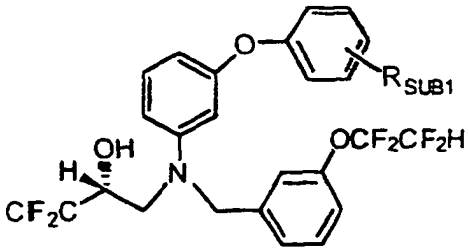
Ex. No.	R_{SUB1}
1139	3-isopropyl
1140	2-Cl, 3-Cl
1141	3-CF_3O
1142	4-F
1143	4-CH_3
1144	2-F, 5-Br
1145	4-Cl, 3-CH_3CH_2
1146	3-CH_3CH_2
1147	3-CH_3, 5-CH_3
1148	3-$(CH_3)_3C$
1149	4-F, 3-CH_3
1150	3-Cl, 4-Cl
1151	3,4-$(CH_2)_4$
1152	3-HCF_2CF_2O
1153	3-CHF_2O
1154	3-$(CH_3)_2N$
1155	3-cyclopropyl
1156	3-(2-furyl)
1157	3-CF_3CF_2
1158	4-NH_2
1159	3-CH_3, 4-CH_3, 5-CH_3
1160	4-$CH_3CH_2CH_2O$
1161	3-CF_3

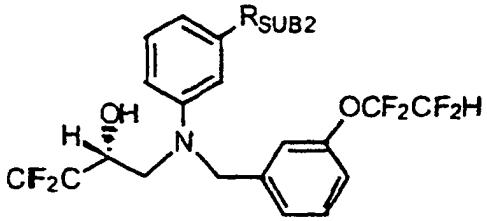
Ex. No.	R_{SUB2}
1163	3-CF_3O-benzyloxy
1164	3-CF_3-benzyloxy
1165	3-F, 5-F-benzyloxy
1166	cyclohexylmethyleneoxy
1167	benzyloxy
1168	3-CF_3, 5-CF_3-benzyloxy
1169	4-CF_3O-benzyloxy
1170	4-CH_3CH_2-benzyloxy
1171	isopropoxy
1172	3-CF_3-benzyl
1173	isopropylthio
1174	cyclopentoxy
1175	3-Cl-5-pyridinyloxy
1176	3-CF_3S-benzyloxy
1177	3-CH_3, 4-CH_3-benzyloxy
1178	2-F, 3-CF_3-benzyloxy
1179	3-F, 5-CF_3-benzyloxy
1180	4-$(CH_3)_2CH$-benzyloxy
1181	1-phenylethoxy
1182	4-F, 3-CH_3-benzoyl
1183	3-CF_3-phenyl
1184	4-CH_3O-phenylamino
1185	cyclopropoxy

Example Table 11 (continued). (2*R*)-3-[*N*-(aryl)-[(aryl)methyl]amino]-1,1-difluoro-1-chloro-2-propanols.

Ex. No.	R_{SUB1}
1162	2-NO_2

Ex. No.	R_{SUB2}
1186	4-NO_2-phenylthio





Ex. No.	R_{SUB1}
1187	3-isopropyl
1188	2-Cl, 3-Cl
1189	3-CF_3O
1190	4-F
1191	4-CH_3
1192	2-F, 5-Br
1193	4-Cl, 3-CH_3CH_2
1194	3-CH_3CH_2
1195	3-CH_3, 5-CH_3
1196	3-$(CH_3)_3C$
1197	4-F, 3-CH_3
1198	3-Cl, 4-Cl
1199	3,4-$(CH_2)_4$
1200	3-HCF_2CF_2O
1201	3-CHF_2O
1202	3-$(CH_3)_2N$
1203	3-cyclopropyl
1204	3-(2-furyl)
1205	3-CF_3CF_2

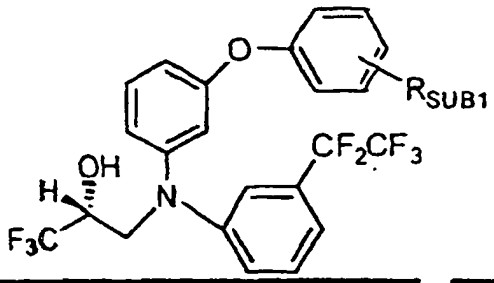
Ex. No.	R_{SUB2}
1211	3-CF_3O-benzyloxy
1212	3-CF_3-benzyloxy
1213	3-F, 5-F-benzyloxy
1214	cyclohexylmethyleneoxy
1215	benzyloxy
1216	3-CF_3, 5-CF_3-benzyloxy
1217	4-CF_3O-benzyloxy
1218	4-CH_3CH_2-benzyloxy
1219	isopropoxy
1220	3-CF_3-benzyl
1221	isopropylthio
1222	cyclopentoxy
1223	3-Cl-5-pyridinyloxy
1224	3-CF_3S-benzyloxy
1225	3-CH_3, 4-CH_3-benzyloxy
1226	2-F, 3-CF_3-benzyloxy
1227	3-F, 5-CF_3-benzyloxy
1228	4-$(CH_3)_2CH$-benzyloxy
1229	1-phenylethoxy

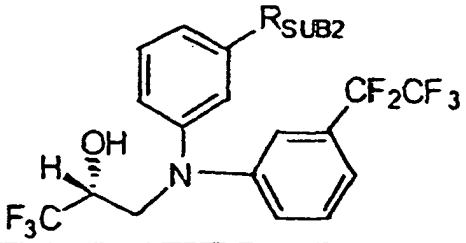
Example Table 11 (continued). (2*R*)-3-[*N*-(aryl)-[(aryl)methyl]amino]-1,1-difluoro-1-chloro-2-propanols.

Ex. No.	R_{SUB1}
1206	4-NH_2
1207	3-CH_3, 4-CH_3, 5-CH_3
1208	4-$CH_3CH_2CH_2O$
1209	3-CF_3
1210	2-NO_2

Ex. No.	R_{SUB2}
1230	4-F, 3-CH_3-benzoyl
1231	3-CF_3-phenyl
1232	4-CH_3O-phenylamino
1233	cyclopropoxy
1234	4-NO_2-phenylthio

Example Table 12. (2*R*)-3-[*N*,*N*'-(diaryl)amino]-1,1,1-trifluoro-2-propanols.
(Included for reference and/or comparison only)





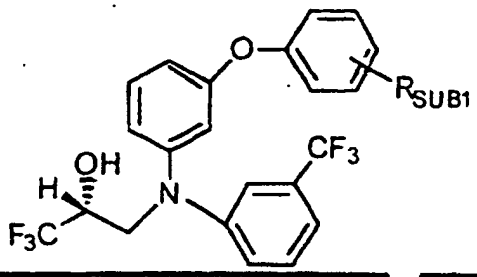
Ex. No.	R_{SUB1}
1235	3-isopropyl
1236	2-Cl, 3-Cl
1237	3-CF_3O
1238	4-F
1239	4-CH_3
1240	2-F, 5-Br
1241	4-Cl, 3-CH_3CH_2
1242	3-CH_3CH_2
1243	3-CH_3, 5-CH_3
1244	3-$(CH_3)_3C$
1245	4-F, 3-CH_3
1246	3-Cl, 4-Cl
1247	3,4-$(CH_2)_4$
1248	3-HCF_2CF_2O
1249	3-CHF_2O
1250	3-$(CH_3)_2N$
1251	3-cyclopropyl
1252	3-(2-furyl)
1253	3-CF_3CF_2
1254	4-NH_2
1255	3-CH_3, 4-CH_3, 5-CH_3
1256	4-$CH_3CH_2CH_2O$
1257	3-CF_3

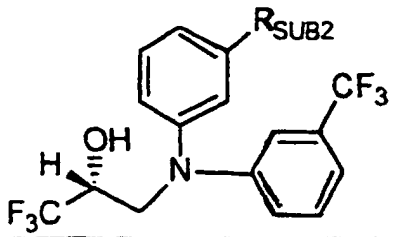
Ex. No.	R_{SUB2}
1259	3-CF_3O-benzyloxy
1260	3-CF_3-benzyloxy
1261	3-F, 5-F-benzyloxy
1262	cyclohexylmethyleneoxy
1263	benzyloxy
1264	3-CF_3, 5-CF_3-benzyloxy
1265	4-CF_3O-benzyloxy
1266	4-CH_3CH_2-benzyloxy
1267	isopropoxy
1268	3-CF_3-benzyl
1269	isopropylthio
1270	cyclopentoxy
1271	3-Cl-5-pyridinyloxy
1272	3-CF_3S-benzyloxy
1273	3-CH_3, 4-CH_3-benzyloxy
1274	2-F, 3-CF_3-benzyloxy
1275	3-F, 5-CF_3-benzyloxy
1276	4-$(CH_3)_2CH$-benzyloxy
1277	1-phenylethoxy
1278	4-F, 3-CH_3-benzoyl
1279	3-CF_3-phenyl
1280	4-CH_3O-phenylamino
1281	cyclopropoxy

Example Table 12 (continued). (2*R*)-3-[*N*,*N*'-(diaryl)amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1258	2-NO_2

Ex. No.	R_{SUB2}
1282	4-NO_2-phenylthio





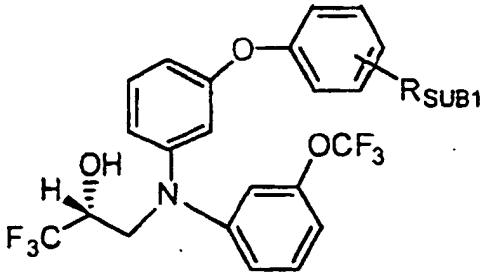
Ex. No.	R_{SUB1}
1283	3-isopropyl
1284	2-Cl, 3-Cl
1285	3-CF_3O
1286	4-F
1287	4-CH_3
1288	2-F, 5-Br
1289	4-Cl, 3-CH_3CH_2
1290	3-CH_3CH_2
1291	3-CH_3, 5-CH_3
1292	3-$(CH_3)_3C$
1293	4-F, 3-CH_3
1294	3-Cl, 4-Cl
1295	3,4-$(CH_2)_4$
1296	3-HCF_2CF_2O
1297	3-CHF_2O
1298	3-$(CH_3)_2N$
1299	3-cyclopropyl
1300	3-(2-furyl)

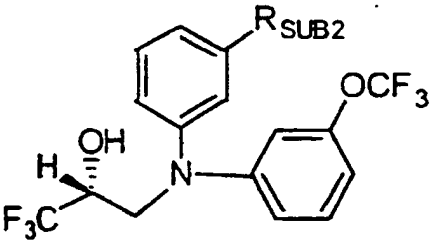
Ex. No.	R_{SUB2}
1307	3-CF_3O-benzyloxy
1308	3-CF_3-benzyloxy
1309	3-F, 5-F-benzyloxy
1310	cyclohexylmethyleneoxy
1311	benzyloxy
1312	3-CF_3, 5-CF_3-benzyloxy
1313	4-CF_3O-benzyloxy
1314	4-CH_3CH_2-benzyloxy
1315	isopropoxy
1316	3-CF_3-benzyl
1317	isopropylthio
1318	cyclopentoxy
1319	3-Cl-5-pyridinyloxy
1320	3-CF_3S-benzyloxy
1321	3-CH_3, 4-CH_3-benzyloxy
1322	2-F, 3-CF_3-benzyloxy
1323	3-F, 5-CF_3-benzyloxy
1324	4-$(CH_3)_2CH$-benzyloxy

Example Table 12 (continued). (2*R*)-3-[*N*,*N*'-(diaryl)amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1301	3-CF_3CF_2
1302	4-NH_2
1303	3-CH_3, 4-CH_3, 5-CH_3
1304	4-$CH_3CH_2CH_2O$
1305	3-CF_3
1306	2-NO_2

Ex. No.	R_{SUB2}
1325	1-phenylethoxy
1326	4-F, 3-CH_3-benzoyl
1327	3-CF_3-phenyl
1328	4-CH_3O-phenylamino
1329	cyclopropoxy
1330	4-NO_2-phenylthio





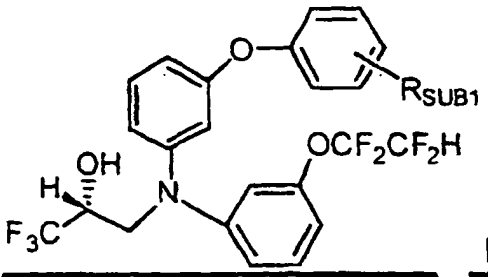
Ex. No.	R_{SUB1}
1331	3-isopropyl
1332	2-Cl, 3-Cl
1333	3-CF_3O
1334	4-F
1335	4-CH_3
1336	2-F, 5-Br
1337	4-Cl, 3-CH_3CH_2
1338	3-CH_3CH_2
1339	3-CH_3, 5-CH_3
1340	3-$(CH_3)_3C$
1341	4-F, 3-CH_3
1342	3-Cl, 4-Cl
1343	3,4-$(CH_2)_4$

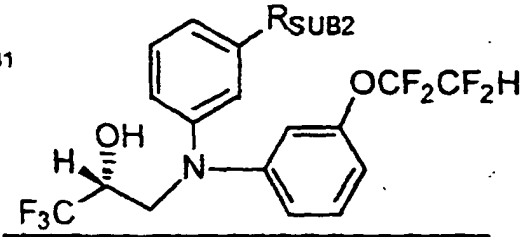
Ex. No.	R_{SUB2}
1355	3-CF_3O-benzyloxy
1356	3-CF_3-benzyloxy
1357	3-F, 5-F-benzyloxy
1358	cyclohexylmethyleneoxy
1359	benzyloxy
1360	3-CF_3, 5-CF_3-benzyloxy
1361	4-CF_3O-benzyloxy
1362	4-CH_3CH_2-benzyloxy
1363	isopropoxy
1364	3-CF_3-benzyl
1365	isopropylthio
1366	cyclopentoxy
1367	3-Cl-5-pyridinyloxy

Example Table 12 (continued). (2*R*)-3-[*N*,*N*'-(diaryl)amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1344	3-HCF_2CF_2O
1345	3-CHF_2O
1346	3-$(CH_3)_2N$
1347	3-cyclopropyl
1348	3-(2-furyl)
1349	3-CF_3CF_2
1350	4-NH_2
1351	3-CH_3, 4-CH_3, 5-CH_3
1352	4-$CH_3CH_2CH_2O$
1353	3-CF_3
1354	2-NO_2

Ex. No.	R_{SUB2}
1368	3-CF_3S-benzyloxy
1369	3-CH_3, 4-CH_3-benzyloxy
1370	2-F, 3-CF_3-benzyloxy
1371	3-F, 5-CF_3-benzyloxy
1372	4-$(CH_3)_2CH$-benzyloxy
1373	1-phenylethoxy
1374	4-F, 3-CH_3-benzoyl
1375	3-CF_3-phenyl
1376	4-CH_3O-phenylamino
1377	cyclopropoxy
1378	4-NO_2-phenylthio





Ex. No.	R_{SUB1}
1379	3-isopropyl
1380	2-Cl, 3-Cl
1381	3-CF_3O
1382	4-F
1383	4-CH_3
1384	2-F, 5-Br
1385	4-Cl, 3-CH_3CH_2
1386	3-CH_3CH_2

Ex. No.	R_{SUB2}
1403	3-CF_3O-benzyloxy
1404	3-CF_3-benzyloxy
1405	3-F, 5-F-benzyloxy
1406	cyclohexylmethyleneoxy
1407	benzyloxy
1408	3-CF_3, 5-CF_3-benzyloxy
1409	4-CF_3O-benzyloxy
1410	4-CH_3CH_2-benzyloxy

Example Table 12 (continued). (2*R*)-3-[*N*,*N*'-(diaryl)amino]-1,1,1-trifluoro-2-propanols.

Ex. No.	R_{SUB1}
1387	3-CH_3, 5-CH_3
1388	3-$(CH_3)_3C$
1389	4-F, 3-CH_3
1390	3-Cl, 4-Cl
1391	3,4-$(CH_2)_4$
1392	3-HCF_2CF_2O
1393	3-CHF_2O
1394	3-$(CH_3)_2N$
1395	3-cyclopropyl
1396	3-(2-furyl)
1397	3-CF_3CF_2
1398	4-NH_2
1399	3-CH_3, 4-CH_3, 5-CH_3
1400	4-$CH_3CH_2CH_2O$
1401	3-CF_3
1402	2-NO_2

Ex. No.	R_{SUB2}
1411	isopropoxy
1412	3-CF_3-benzyl
1413	isopropylthio
1414	cyclopentoxy
1415	3-Cl-5-pyridinyloxy
1416	3-CF_3S-benzyloxy
1417	3-CH_3, 4-CH_3-benzyloxy
1418	2-F, 3-CF_3-benzyloxy
1419	3-F, 5-CF_3-benzyloxy
1420	4-$(CH_3)_2CH$-benzyloxy
1421	1-phenylethoxy
1422	4-F, 3-CH_3-benzoyl
1423	3-CF_3-phenyl
1424	4-CH_3O-phenylamino
1425	cyclopropoxy
1426	4-NO_2-phenylthio

BIOASSAYS

CETP Activity *In Vitro*

ASSAY OF CETP INHIBITION USING PURIFIED COMPONENTS (RECONSTITUTED BUFFER ASSAY)

[0233] The ability of compounds to inhibit CETP activity was assessed using an *in vitro* assay that measured the rate of transfer of radiolabeled cholesteryl ester ([^{3}H]CE) from HDL donor particles to LDL acceptor particles. Details of the assay are provided by Glenn. K. C. et al. (Glenn and Melton, "Quantification of Cholesteryl Ester Transfer Protein (CETP): A) CETP Activity and B) Immunochemical Assay of CETP Protein," *Meth. Enzymol.*, 263, 339-351 (1996)). Human recombinant CETP can be obtained from the serum-free conditioned medium of CHO cells transfected with a cDNA for CETP and purified as described by Wang, S. et al. (*J. Biol. Chem. 267*, 17487-17490 (1992)). To measure CETP activity, [^{3}H]CE-labeled-HDL, LDL, CETP and assay buffer (50 mM tris(hydroxymethyl)aminomethane, pH 7.4: 150 mM sodium chloride; 2 mM ethylenediamine-tetraacetic acid (EDTA); 1% bovine serum albumin) were incubated in a final volume of 200 µL, for 2 hours at 37 °C in 96 well plates. Inhibitors were included in the assay by diluting from a 10 mM DMSO stock solution into 16% (v/v) aqueous DMSO so that the final concentration of inhibitor was 800 µM. The inhibitors were then diluted 1:1 with CETP in assay buffer, and then 25 µL of that solution was mixed with 175 µL of lipoprotein pool for assay. Following incubation, LDL was differentially precipitated by the addition of 50 µL of 1% (w/v) dextran sulfate/0.5 M magnesium chloride, mixed by vortex, and incubated at room temperature for 10 minutes.

A potion of the solution (200 µL) was transferred to a filter plate (Millipore). After filtration, the radioactivity present in the precipitated LDL was measured by liquid scintillation counting. Correction for non-specific transfer or precipitation was made by including samples that do not contain CETP. The rate of [^{3}H]CE transfer using this assay was linear with respect to time and CETP concentration. up to 25-30% of [^{3}H]CE transferred.

[0234] The potency of test compounds was determined by performing the above described assay in the presence of varying concentrations of the test compounds and determining the concentration required for 50% inhibition of transfer of [^{3}H]CE from HDL to LDL. This value was defined as the IC_{50}. The IC_{50} values determined from this assay are accurate when the IC_{50} is greater than 10 nM. In the case where compounds have greater inhibitory potency, accurate measurements of IC_{50} may be determined using longer incubation times (up to 18 hours) and lower final concentrations of CETP (< 50 nM).

[0235] Examples of IC_{50} values determined by these methods are summarized in Table 9.

ASSAY OF CETP INHIBITION IN HUMAN PLASMA

[0236] Blood was obtained from healthy volunteers. recruited from the personnel of Monsanto Company, Saint Louis, MO. Blood was collected in tubes containing EDTA (EDTA plasma pool). The EDTA human plasma pool. previously stored at -20 °C, was thawed at room temperature and centrifuged for 5 minutes to remove any particulate matter. Tritiated HDL, radiolabeled in the cholesteryl ester moiety ([^{3}H]CE-HDL) as described by Morton and Zilversmit (J. Biol. Chem., 256, 11992-95 (1981)), was added to the plasma to a final concentration of 25 µg/mL cholesterol. Equal volumes (396 µL) of the plasma containing the [^{3}H]CE-HDL were added by pipette into micro tubes (Titertube®, Bio-Rad laboratories, Hercules, CA). Inhibitor compounds, dissolved as 20-50 mM stock solutions in DMSO, were serially diluted in DMSO (or an alternative solvent in some cases. such as dimethylformamide or ethanol). Four µL of each of the serial dilutions of inhibitor compounds or DMSO alone were then added to each of the tubes containing plasma (396 µL). After mixing, triplicate aliquots (100 µL) from each plasma tube were then transferred to wells of 96-well roundbottomed polystyrene microtiter plates (Corning, Corning, NY). Plates were sealed with plastic film and incubated at 37 °C for 4 hours. "Test" samples contained plasma with dilutions of inhibitor compounds. "Control" samples contained plasma with DMSO diluted to the same concentration as the test samples. but without inhibitor. "Blank" samples were prepared as "control" samples, but were left in the micro tubes at 4 °C for the 4 hour incubation and were then added to the microtiter wells at the end of the incubation period. VLDL and LDL were precipitated by the addition of 10 µL of precipitating reagent (1% (w/v) dextran sulfate (Dextralip50)/0.5 M magnesium chloride, pH 7.4) to all wells. The wells were mixed on a plate mixer and then incubated at ambient temperature for 10 min. The plates were then centrifuged at 1000 x g for 30 min at 10 °C. The supernatants (50 µL) from each well were then transferred to Picoplate™ 96 plate wells (Packard. Meriden, CT) containing Microscint™-40 (Packard, Meriden, CT). The plates were heat-sealed (TopSeal™-P, Packard, Meriden, CT) according to the manufacturer's directions and mixed for 30 min. Radioactivity was measured on a microplate scintillation counter (TopCount, Packard, Meriden, CT). The maximum percentage transfer in the control wells (% transfer) was determined using the following equation:

$$\% \text{ Transfer} = \frac{[dpm_{blank} - dpm_{control}] \times 100}{dpm_{blank}}$$

[0237] The percentage of transfer relative to the control (% control) was determined in the wells containing inhibitor compounds was determined as follows:

$$\% \text{ Control} = \frac{[dpm_{blank} - dpm_{test}] \times 100}{dpm_{blank} - dpm_{control}}$$

[0238] IC_{50} values were then calculated from plots of % control versus concentration of inhibitor compound. IC_{50} values were determined as the concentration of inhibitor compound inhibiting transfer of [^{3}H]CE from the supernatant [^{3}H]CE-HDL to the precipitated VLDL and LDL by 50% compared to the transfer obtained in the control wells.

[0239] Examples of plasma IC_{50} values determined by these methods are summarized in Table 10.

ASSAY OF CETP INHIBITION *IN VIVO*.

[0240] Inhibition of CETP activity by a test compound can be determined by administering the compound to an animal by intravenous injection or oral gavage, measuring the amount of transfer of tritium-labeled cholesteryl ester ([^{3}H]CE) from HDL to VLDL and LDL particles, and comparing this amount of transfer with the amount of transfer observed in

control animals.

[0241] Male golden Syrian hamsters were maintained on a diet of chow containing 0.24% cholesterol for at least two weeks prior to the study. For animals receiving intravenous dosing immediately before the experiment, animals were anesthetized with pentobarbital. Anesthesia was maintained throughout the experiment. In-dwelling catheters were inserted into the jugular vein and carotid artery. At the start of the experiment all animals received 0.2 mL of a solution containing [^{3}H]CE-HDL into the jugular vein. [^{3}H]CE-HDL is a preparation of human HDL containing tritium-labeled cholesteryl ester, and was prepared according to the method of Glenn et al. (*Meth. Enzymol.*, 263, 339-351 (1996)). Test compound was dissolved as a 80 mM stock solution in vehicle (2% ethanol: 98% PEG 400, Sigma Chemical Company, St. Louis, Missouri, USA) and administered either by bolus injection or by continuous infusion. Two minutes after the [^{3}H]CE-HDL dose was administered, animals received 0.1 mL of the test solution injected into the jugular vein. Control animals received 0.1 mL of the intravenous vehicle solution without test compound. After 5 minutes, the first blood samples (0.5 mL) were taken from the carotid artery and collected in standard microtainer tubes containing ethylenediamine tetraacetic acid. Saline (0.5 mL) was injected to flush the catheter and replace blood volume. Subsequent blood samples were taken at two hours and four hours by the same method. Blood samples were mixed well and kept on ice until the completion of the experiment. Plasma was obtained by centrifugation of the blood samples at 4 °C. The plasma (50 µL) was treated with 5 µL of precipitating reagent (dextran sulfate, 10 g/L: 0.5 M magnesium chloride) to remove VLDL/LDL. After centrifugation, the resulting supernatant (25 µL) containing the HDL was analyzed for radioactivity using a liquid scintillation counter.

[0242] The percentage [^{3}H]CE transferred from HDL to LDL and VLDL (% transfer) was calculated based on the total radioactivity in equivalent plasma samples before precipitation. Typically, the amount of transfer from HDL to LDL and VLDL in control animals was 20% to 35% after 4 hours. The polyethylene glycol vehicle was determined to have no effect on CETP activity in this model.

[0243] Alternatively, conscious, non-anesthetized animals received an oral gavage dose of test compound as a suspension in 0.1% methyl cellulose in water. At a time determined for each compound at which plasma levels of the test substance reached their peak (C_{max}) after oral dosing, the animals were anesthetized with pentobarbital and then dosed with 0.2 mL of a solution containing [^{3}H]CE-HDL into the jugular vein as described above. Control animals received 0.25 mL of the vehicle solution without test compound by oral gavage. After 4 hours, the animals were sacrificed, blood samples were collected, and the percentage [^{3}H]CE transferred from HDL to LDL and VLDL (% transfer) assayed, as described above. The aqueous methyl cellulose vehicle was determined to have no effect on CETP activity in this model. Results from testing in this model are summarized in Table 11.

[0244] Alternatively, inhibition of CETP activity by a test compound was determined by administering the compound to mice which have been selected for expression of human CETP (hCETP) by transgenic manipulation (hCETP mice). Test compounds were administered by intravenous injection, or oral gavage and the amount of transfer of tritium-labeled cholesteryl ester ([^{3}H]CE) from HDL to VLDL and LDL particles was determined, and compared to the amount of transfer observed in control animals. C57Bl/6 mice that were homozygous for the hCETP gene were maintained on a high fat chow diet, such as TD 88051, as described by Nishina et al. (J Lipid Res., 31, 859-869 (1990)) for at least two weeks prior to the study. Mice received an oral gavage dose of test compound as a suspension in 0.1% methyl cellulose in water or an intravenous bolus injection of test compound in 10% ethanol and 90% polyethylene glycol. Control animals received the vehicle solution without test compound by oral gavage or by an intravenous bolus injection. At the start of the experiment all animals received 0.05 mL of a solution containing [^{3}H]CE-HDL into the tail vein. [^{3}H]CE-HDL is a preparation of human HDL containing tritium-labeled cholesteryl ester, and was prepared according to the method of Glenn et al. (*Meth. Enzymol.*, 263, 339-351 (1996)). After 30 minutes, the animals were exsanguinated and blood collected in standard microtainer tubes containing ethylenediamine tetraacetic acid. Blood samples were mixed well and kept on ice until the completion of the experiment. Plasma was obtained by centrifugation of the blood samples at 4 °C. The plasma was separated and analyzed by gel filtration chromatography and the relative proportion of [^{3}H]CE in the VLDL. LDL and HDL regions was determined.

[0245] The percentage [^{3}H]CE transferred from HDL to LDL and VLDL (% transfer) was calculated based on the total radioactivity in equivalent plasma samples before precipitation. Typically, the amount of transfer from HDL to LDL and VLDL in control animals was 20% to 35% after 30 min. The polyethylene glycol and the aqueous methyl cellulose vehicles were determined to have no effect on CETP activity in this model. Results from testing in this model are summarized in Table 12.

ASSAY OF PLASMA HDL ELEVATION *IN VIVO*.

[0246] Syrian Golden hamsters were made hypercholesterolemic by feeding cholesterol supplemented chow for a minimum of two weeks, as described above. Test compounds were administered orally in selected aqueous or oil based vehicles for up to 1 week. Serum was obtained and analyzed by precipitation or size exclusion chromatography for the relative abundance of VLDL, LDL and HDL. Results from testing in this model are summarized in Table 13.

[0247] Alternatively, a strain of C57bl mouse was made to transgenicaly express human CETP. Plasma concentrations of hCETP ranged from 2-20 μg/ml. The hCETP mice were made hyperchotesterolemic by feeding cholesterol and fat supplemented chow for a minimum of two weeks. as described above. Test compounds were administered orally in selected aqueous or oil based vehicles for up to 1 week. Serum was obtained and analyzed by size exclusion chromatography for the relative abundance of VLDL, LDL and HDL. Results from testing in this model are summarized in Table 14.

[0248] Alternatively, cynomologous monkeys were maintained on a normal chow diet. The compound corresponding to example 8 was dissolved in a corn oil based vehicle and administered by oral gavage at 10 mpk q.d. for up to 11 days. Plasma levels of drug were detected throughout the experiment in treated animals at ranges of 0.1-1.5 μg/mL. Periodically, plasma samples were taken and analyzed for total cholesterol and HDL. After seven days, the treated animals exhibited a 2% increase in HDL and a 5% increase in total cholesterol, relative to vehicle-treated controls.

[0249] Alternatively, rabbits were maintained on a normal chow diet. The compound corresponding to example 8 was dissolved in a vehicle of ethanol:propylene glycol (1.5:18) and administered by Alzet pump at 30 mg/day/animal for up to 14 days. Plasma concentrations of drug were detected throughout the duration of the pump infusion in treated animals and averaged 1.2 μg/mL. Periodically, plasma samples were taken and analyzed for triglycerides, total cholesterol, and HDL. After fourteen days, the treated animals exhibited a 12% decrease in HDL, a 19% decrease in total cholesterol, as well as a 17% increase in triglycerides, compared to pre-dose levels.

Table 9. Inhibition of CETP Activity by Examples in Reconstituted Buffer Assay.

Ex. No.	IC_{50} (μM)	Ex. No.	IC_{50} (μM)
8	0.0008	42	0.38
11	0.001	27	0.44
19	0.004	26	0.53
9	0.008	29	0.72
10	0.012	3*	0.76
2	0.014	28	0.86
4	0.014	32	1.2
20	0.027	25	1.4
22	0.027	39	1.6
12	0.034	15	1.6
14	0.04	30	2.7
18	0.044	33B	3.2
16	0.049	5	3.4
43	0.058	31	3.5
23	0.066	7	4.9
34	0.076	44*	6.8
41	0.086	17	18
21	0.11	6*	68
13	0.13	44A*	> 50
1	0.14		
33	0.15		
38	0.18		
36	0.20		
37	0.21		
40	0.23		
35	0.28		
24	0.33		

*Included for reference and/or comparison only.

Table 10.

Inhibition of CETP Activity by Examples in Human Plasma Assay.	
Ex. No.	IC_{50} (μM)
8	0.049
11	0.072
10	0.11
22	0.14
19	0.19
20	0.3
18	0.44
14	0.59
9	0.62
2	0.65
4	0.65
16	0.77
12	0.79
34	1.4
43	1.5
23	2.0
1	5.6
41	7.2
42	11
3*	20

*Included for reference and/or comparison only.

Table 11.

Inhibition of CETP-mediated Transfer in Hamster		
Ex. No.	**Single Oral Dose**	**% Inhibition of Transfer**
8	10 mpk	35

Table 12.

Inhibition of CETP-mediated Transfer in hCETP Mice.		
Ex. No.	**Single Oral Dose**	**% Inhibition of Transfer**
8	60 mpk	40

Table 13.

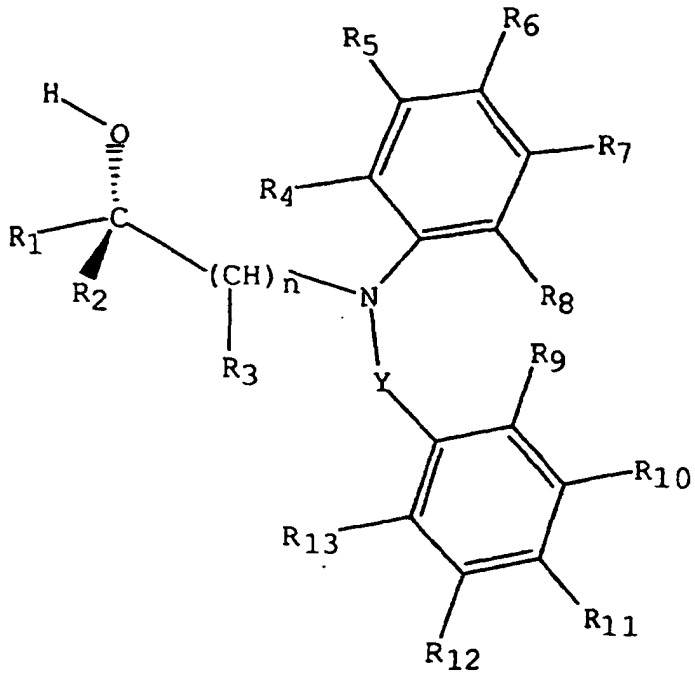
Change in Lipoprotein Profile in Hamster.				
Ex. No.	**Oral Dose qd, 5 days**	**% Change in Lipoprotein Profile**		
		HDL	**LDL**	**VLDL**
8	30 mpk	12	-12	-22

Table 14.

Change in Lipoprotein Profile in hCETP Mice.				
Ex. No.	**Oral Dose qd, 5 days**	**% Change in Lipoprotein Profile**		
		HDL	**LDL**	**VLDL**
8	30 mpk	12	20	-

Claims

1. Compound of Formula M:



(M)

or a pharmaceutically acceptable salt thereof, wherein;
n is selected from the integers 1, 2, 3 and 4;
Y is $-(CH_2)_q-$ wherein q is 1 or 2;
R_1 is haloalkyl;
R_2 is hydrido;
R_3 is hydrido;
R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, haloalkyl, and alkyl;

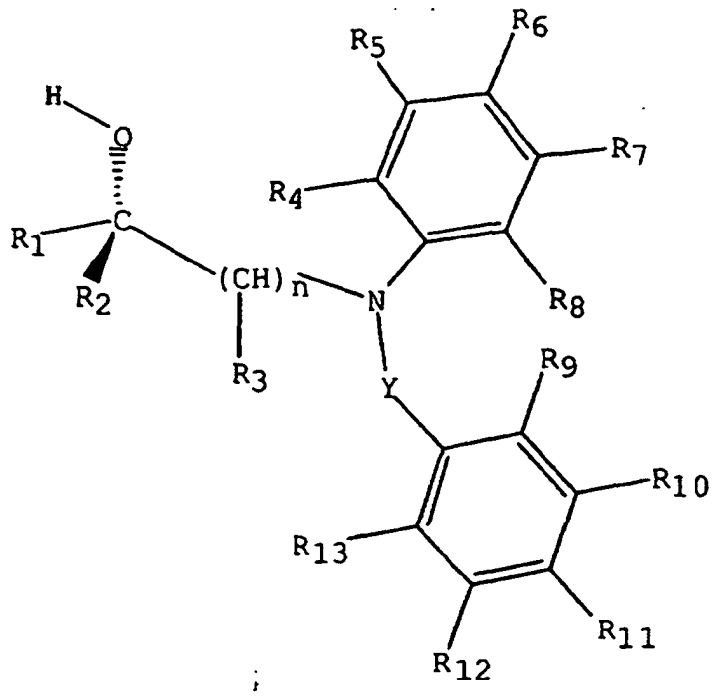
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydride, carboxy, heteroaralkylthio, heteroaralkoxy, cycloalkylamino, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, aralkenyl, aralkynyl, heterocyclyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, aralkylsulfinyl, aralkylsulfinylalkyl, halocycloalkyl, halocycloalkenyl, cycloalkylsulfinyl, cycloalkylsulfinylalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, heteroarylamino, N-heteroarylamino-N-alkylamino, heteroarylaminoalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkenyloxy, cycloalkoxyalkyl, cycloalkylalkoxy, cycloalkenyloxyalkyl, halocycloalkoxy, halocycloalkoxyalkyl, halocycloalkenyloxy, halocycloalkenyloxyalkyl, hydroxy, amino, thio, nitro, C1-C6 alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, heteroaralkoxyalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, arylsulfonylalkyl, heteroarylsulfinylalkyl, heteroarylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfinylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylamidosulfonyl, arylsulfonamido, alkylarylamidosulfonyl, arylsulfinyl, arylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, heterocyclylsulfonyl, heterocyclylthio, alkanoyl, alkenoyl, aroyl, heteroaroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, cycloalkyl, cycloalkylalkanoyl, cycloalkenyl, C3-C7 cycloalkylalkyl, C3-C7 cycloalkenylalkyl, halo, haloalkyl, haloalkenyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, hydoxyheteroaralkyl, haloalkoxyalkyl, aryl, heteroaralkynyl, aryloxy, aralkoxy, aryloxyalkyl, saturated heterocyclyl, partially saturated heterocyclyl, heteroaryl, heteroaryloxy, heteroaryloxyalkyl, heteroaralkyl, arylalkenyl, heteroarylalkenyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalkoxyalkyl, carboalkoxyalkenyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cyano, cycloalkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl, haloalkylthio, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, halocycloalkyl, halocycloalkenyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, haloalkoxylalkyl, cycloalkoxy, cycloalkoxyalkyl, cycloallcylalkoxy, hydroxy, thio, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylthioalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosutfonyl, amidosulfonyl, monoalkyl amidosulfonyl, dialkyl amidosulfonyl, arylsulfonyl, alkenoyl, aroyl, aralkanoyl, haloalkanoyl, alkenyl, alkynyl, alkenyloxy, alkenyloxyalky, cycloalkylalkanoyl, C3-C7 cycloalkylalkyl, haloalkenyl, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, haloalkoxyalkyl, aryl, aralkyl, aryloxy, aralkoxy, aryloxyalkyl, carboxyalkyl, carboalkoxy, alkoxycarbonyl, carboaralkoxy, carboxamido, carboxamidoalkyl, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl,

with the proviso that at least one of R_4, R_5, R_6, R_7, and R_8 is not hydrido,

and with the further proviso that at least one of R_9, R_{10}, R_{11}, R_{12}, and R_{13} is not hydrido.

2. Compound of Claim 1 of Formula M:



(M)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 3;

Y is $-(CH_2)_q-$ wherein q is 1 or 2;

R_1 is haloalkyl;

R_2 is hydrido;

R_3 is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydride, halo, and haloalkyl;

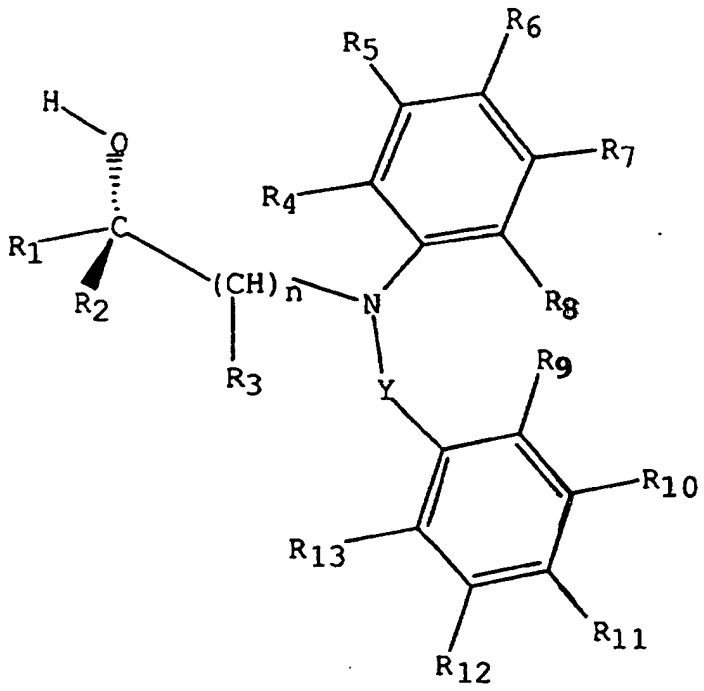
R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, heteroaralkoxy, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, perhaloaralkyl, aralkylsulfonyl, aralkylsulfonylalkyl, halocycloalkyl, cycloalkylsulfonyl, cycloalkylsulfonylalkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxy, halocycloalkoxy, halocycloalkoxyalkyl, hydroxy, amino, nitro, C1-C6 alkylamino, alkylthio, alkylthioalkyl, arylamino, aralkylamino, arylthio, arylsulfonylalkyl, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylsulfonyl, alkanoyl, aroyl, aralkanoyl, heteroaralkanoyl, haloalkanoyl, alkyl, cycloalkyl, cycloalkylalkanoyl, C3-C7 cycloalkylalkyl, halo, haloalkyl, haloalkoxy, hydroxyhaloalkyl, hydroxyaralkyl, hydroxyalkyl, haloalkoxyalkyl, aryl, aryloxy, aralkoxy, aryloxyalkyl, heteroaryloxy, heteroaryloxyalkyl, carboxyalkyl, carboalkoxy, alkoxycarboxamido, carboalkoxyalkyl, carboaralkoxy, carboxamido, carboxamidoalkyl, cyano, carbohaloalkoxy, phosphono, phosphonoalkyl, diaralkoxyphosphono, and diaralkoxyphosphonoalkyl;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cyano, cycloalkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl and haloalkylthio,

with the proviso that at least one of R_4, R_5, R_6, R_7, and R_8 is not hydrido

and with the further proviso that at least one of R_9, R_{10}, R_{11}, R_{12}, and R_{13} is not hydrido.

3. Compound of Claim 2 of Formula M:



(M)

or a pharmaceutically acceptable salt thereof, wherein;

n is an integer selected from 1 through 3;

Y is $-(CH_2)_q-$ wherein q is 1 or 2;

R_1 is haloalkyl;

R_2 is hydrido;

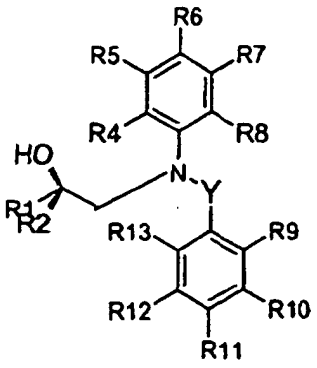
R_3 is hydrido;

R_4, R_8, R_9, and R_{13} are independently selected from the group consisting of hydrido, halo, and haloalkyl;

R_5, R_6, R_7, R_{10}, R_{11}, and R_{12} are independently selected from the group consisting of hydrido, heteroaralkoxy, acylalkyl, acylalkoxy, aroylalkoxy, heterocyclyloxy, aralkylaryl, aralkyl, perhaloaralkyl, haloalkylthio, alkanoyloxy, alkoxy, alkoxyalkyl, heteroaralkoxy, cycloalkoxy, cycloalkoxyalkyl, cycloalkylalkoxy, halocycloalkoxy, halocycloalkoxyalkyl, alkylthio, alkylthioalkyl, arylthio, alkylsulfonyl, alkylsulfonylalkyl, haloalkylsulfonylalkyl, alkylsulfonamido, alkylaminosulfonyl, amidosulfonyl, alkylamidosulfonyl, arylsulfonyl, alkanoyl, haloalkanoyl, alkyl, cycloalkyl, C3-C7 cycloalkylalkyl, halo, haloalkyl, haloalkoxy, haloalkoxyalkyl, aryl, aryloxy, aralkoxy, aryloxyalkyl, heteroaryloxy, heteroaryloxyalkyl, carboalkoxy, carboalkoxyalkyl, carboaralkoxy and carbohaloalkoxy;

further, wherein when R_7 is aryloxy or aralkoxy, said aryloxy or aralkoxy may be substituted at one or more substitutable positions with one or more radicals selected from amino, halo, nitro, alkoxy, alkyl, cycloalkoxy, cycloalkyl, cycloalkylalkoxy, haloalkoxy, C1-C6 alkylamino, haloalkyl, alkanoyl and haloalkylthio.

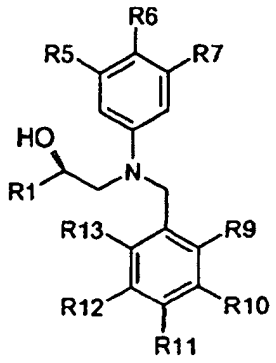
4. Compound of Claim 3 of Formula "D"



Formula "D"

wherein Y is $-CH_2-$;
wherein R^1 is haloalkyl;
wherein R^2 is hydrido;
wherein R^4 and R^8 are hydrido;
wherein R^5 and R^6 are selected from hydrido and alkoxy;
wherein R^7 is selected from aryloxy, arylalkoxy, 5,6,7,8-tetrahydronaphth-2-yloxy, alkoxy, cycloalkoxy, cycloalkylalkoxy and halo;
wherein said aryloxy and arylalkoxy groups in R^7 may be substituted at one or more substitutable positions with one or more radicals selected from halo, alkyl, alkoxy, haloalkoxy and haloalkyl;
wherein R^9 is selected from hydrido, halo and haloalkyl;
wherein R^{10} is selected from haloalkoxy, haloalkyl and haloalkylthio;
wherein R^{11} is selected from hydrido, halo and haloalkyl;
wherein R^{12} is selected from hydrido and haloalkyl;
wherein R^{13} is selected from hydrido, halo and haloalkyl.

5. Compound of Claim 4 of formula "C"



Formula "C"

wherein R^1 is selected from trifluoromethyl and chloromethyl;
wherein R^5 and R^6 are selected from hydrido and methoxy;
wherein R^7 is selected from phenyloxy, benzyloxy, 5,6,7,8-tetrahydronaphth-2-yloxy, isopropoxy, cyclopentoxy, bromo, cyclohexylmethoxy and methoxy;
wherein said phenyloxy and benzyloxy groups in R^7 may be substituted at one or more substitutable positions with one or more radicals selected from chloro, ethyl, trifluoromethoxy, bromo, fluoro, methyl, isopropyl, trifluoromethyl, isopropoxy and tert-butyl;

wherein R^9 is selected from hydrido, fluoro and trifluoromethyl;
wherein R^{10} is selected from 1,1,2,2-tetrafluoroethoxy, trifluoromethoxy, pentafluoroethyl, trifluoromethyl and trifluoromethylthio;
wherein R^{11} is selected from hydrido, trifluoromethyl and fluoro;
wherein R^{12} is selected from hydrido and trifluoromethyl;
wherein R^{13} is selected from hydrido, fluoro and trifluoromethyl.

6. Compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein said compound is selected from the group consisting of:

(2R)-3-[[3-(3-trifluoromethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(3-isopropylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-methylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(2-bromo-5-fluorophenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy) phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(phenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoromethoxy)-phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoromethyl)-phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3,5-difluorophenyl]-methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-isopropoxyphenyl][[3-(1,1,2,2-tetrafluoroethoxy)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(pentafluoroethyl)phenyl]methyl]-amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[2-fluoro-5-(trifluoromethyl)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[2-fluoro-4-(trifluoromethyl)-phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol;

(2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(trifluoromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol.

(2R)-3-[[3-(3-(trifluoromethoxy)phenoxy)phenyl][[3-(trifluromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol.

(2R)-3-[[3-(4-methylphenoxy)phenyl][[3-(trifluromethoxy)phenyl]methyl]amino]-1,1,1-trifluoro-2-propanol.

7. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

8. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[(3-phenoxyphenyl)[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl]amino]- 1,1,1-trifluoro-2-propanol.

9. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(4-methylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

10. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(3-isopropylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

11. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(3-ethylphenoxy)phenyl][[3-(1;1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

12. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(3-trifluoromethoxylphenoxy)phenyl][[3-(1,1,2,2-tetrafluoroethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

13. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2R)-3-[[3-(4-chloro-3-ethylphenoxy)phenyl][[3-(trifluoromethoxy)phenyl]-methyl]amino]-1,1,1-trifluoro-2-propanol.

14. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoromethyl)phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol.

15. Compound of Claim 6, or a pharmaceutically acceptable salt thereof, wherein said compound is (2*R*)-3-[[[3-(1,1,2,2-tetrafluoroethoxy)phenyl]methyl][3-[[3-(trifluoromethoxy)phenyl]methoxy]phenyl]amino]-1,1,1-trifluoro-2-propanol.

16. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier.

17. The use of compound of Claim 1 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for treating or preventing a CETP-mediated disorder in a subject.

18. The use of Claim 17 wherein the treating of a CETP-mediated disorder is coronary artery disease.

19. The use of Claim 17 wherein the preventing of a CETP-mediated disorder is coronary artery disease.

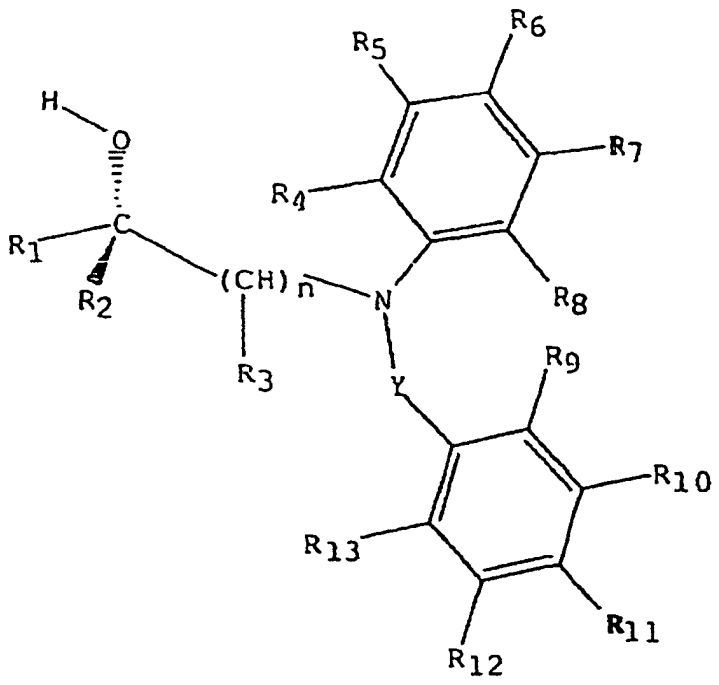
20. The use of Claim 17 wherein the preventing of a CETP-mediated disorder is preventing cerebral vascular accident (CVA).

21. The use of Claim 17 wherein the treating of a CETP-mediated disorder is treating dyslipidemia.

22. The use of Claim 17 wherein the preventing of a CETP-mediated disorder is preventing dyslipidemia.

Patentansprüche

1. Verbindung der Formel M:

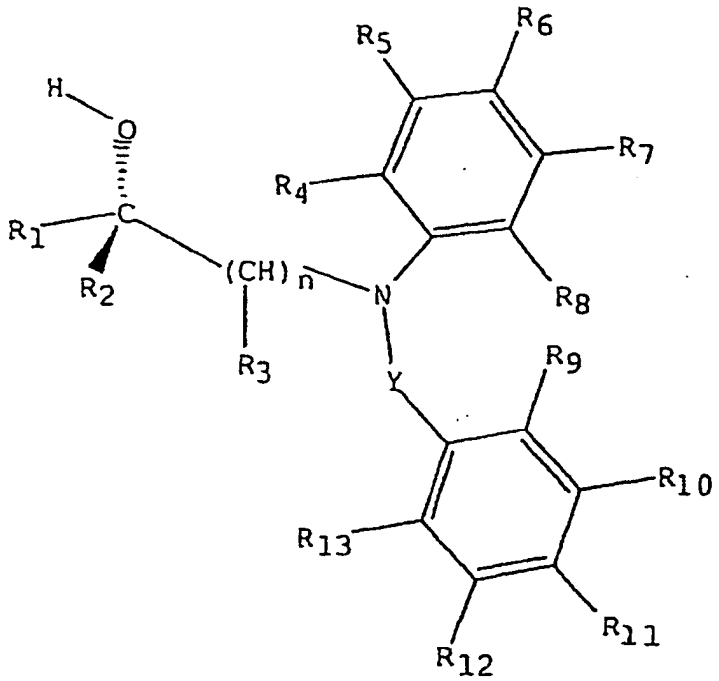


(M)

oder ein pharmazeutisch annehmbares Salz davon, worin
n aus den ganzen Zahlen 1, 2, 3 und 4 ausgewählt ist;
Y für $-(CH_2)_q-$ steht, wobei q den Wert 1 oder 2 hat;
R_1 für Halogenalkyl steht;
R_2 für Hydrido steht;
R_3 für Hydrido steht,
R_4, R_8, R_9 und R_{13} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Halogen, Halogenalkyl und Alkyl, ausgewählt sind,
R_5, R_6, R_7, R_{10}, R_{11} und R_{12} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Carboxy, Heteroaralkylthio, Heteroaralkoxy, Cycloalkylamino, Acylalkyl, Acylalkoxy, Aroylalkoxy, Heterocyclyloxy, Aralkylaryl, Aralkyl, Aralkenyl, Aralkinyl, Heterocyclyl, Perhalogenaralkyl, Aralkylsulfonyl, Aralkylsulfonylalkyl, Aralkylsulfinyl, Aralkylsulfinylalkyl, Halogencycloalkyl, Halogencycloalkenyl, Cycloalkylsulfinyl, Cycloalkylsulfinylalkyl, Cycloalkylsulfonyl, Cycloalkylsulfonylalkyl, Heteroarylamino, N-Heteroarylamino-N-alkylamino, Heteroarylaminoalkyl, Halogenalkylthio, Alkanoyloxy, Alkoxy, Alkoxyalkyl, Heteroaralköxy, Cycloalkoxy, Cycloalkenyloxy, Cycloalkoxyalkyl, Cycloalkylalkoxy, Cycloalkenyloxyalkyl, Halogencycloalkoxy, Halogencycloalkoxyalkyl, Halogencycloalkenyloxy, Halogencycloalkenyloxyalkyl, Hydroxy, Amino, Thio, Nitro, C_1-C_6-Alkylamino, Alkylthio, Alkylthioalkyl, Arylamino, Aralkylamino, Arylthio, Arylthioalkyl, Heteroaralkoxyalkyl, Alkylsulfinyl, Alkylsulfinylalkyl, Arylsulfinylalkyl, Arylsulfonylalkyl, Heteroarylsulfinylalkyl, Heteroarylsulfonylalkyl, Alkylsulfonyl, Alkylsulfonylalkyl, Halogensulfinylalkyl, Halogenalkylsulfonylalkyl, Alkylsulfonamido, Alkylaminosulfonyl, Amidosulfonyl, Alkylamidosulfonyl, Arylamidosulfonyl, Arylsulfonamido, Alkylarylamidosulfonyl, Arylsulfinyl, Arylsulfonyl, Heteroarylthio, Heteroarylsulfinyl, Heteroarylsulfonyl, Heterocyclylsulfonyl, Heterocyclylthio, Alkanoyl, Alkenoyl, Aroyl, Heteroaroyl, Aralkanoyl, Heteroaralkanoyl, Halogenalkanoyl, Alkyl, Alkenyl, Alkinyl, Alkenyloxy, Alkenyloxyalkyl, Cycloalkyl, Cycloalkylalkanoyl, Cycloalkenyl, C_3-C_7-Cycloalkylalkyl, C_3-C_7-Cycloalkenylalkyl, Halogen, Halogenalkyl, Halogenalkenyl, Halogenalkoxy, Hydroxyhalogenalkyl, Hydroxyaralkyl, Hydroxyalkyl, Hydroxyheteroaralkyl, Halogenalkoxyalkyl, Aryl, Heteroaralkinyl, Aryloxy, Aralkoxy, Aryloxyalkyl, gesättigtem Heterocyclyl, teilweise gesättigtem Heterocyclyl, Heteroaryl, Heteroaryloxy, Heteroaryloxyalkyl, Heteroaralkyl, Arylalkenyl, Heteroarylalkenyl, Carboxyalkyl, Carboxyalkoxy, Alkoxycarboxamido, Alkylamidocarbonylamido, Arylamidocarbonylamido, Carboalkoxyalkyl, Carboalkoxyalkenyl, Carboaralkoxy, Carboxamido, Carboxamidoalkyl, Cyano, Carbohalogenalkoxy, Phosphono, Phosphonoalkyl, Diaralkoxyphosphono und Diaralkoxyphosphonoalkyl, ausgewählt sind;
wobei weiterhin, wenn R_7 für Aryloxy oder Aralkoxy steht, das genannte Aryloxy oder Aralkoxy an einer oder mehreren substituierbaren Positionen mit einem oder mehreren Resten, ausgewählt aus Amino, Halogen, Nitro,

Alkoxy, Alkyl, Cyano, Cycloalkoxy, Cycloalkyl, Cycloalkylalkoxy, Halogenalkoxy, C_1-C_6-Alkylamno, Halogenalkyl, Alkanoyl, Halogenalkylthio, Perhalogenaralkyl, Aralkylsulfonyl, Aralkylsulfonylalkyl, Halogencycloalkyl, Halogencycloalkenyl, Halogenalkylthio, Alkanoyloxy, Alkoxy, Alkoxyalkyl, Halogenalkoxyalkyl, Cycloalkoxy, Cycloalkoxyalkyl, Cycloalkylalkoxy, Hydroxy, Thio, Alkylthio, Alkylthioalkyl, Arylamino, Aralkylamino, Arylthio, Arylthioalkyl, Alkylsulfonyl, Alkylsulfonylalkyl, Halogenalkylsulfonylalkyl, Alkylsulfonamido, Alkylaminosulfonyl, Amidosulfonyl, Monoalkylamidosulfonyl, Dialkylamidosulfonyl, Arylsulfonyl, Alkenoyl, Aroyl, Aralkanoyl, Halogenalkanoyl, Alkenyl, Alkinyl, Alkenyloxy, Alkenyloxyalkyl, Cycloalkylalkanoyl, C_3-C_7-Cycloalkylalkyl, Halogenalkenyl, Hydroxyhalogenalkyl, Hydroxyaralkyl, Hydroxyalkyl, Halogenalkoxyalkyl, Aryl, Aralkyl, Aryloxyl, Aralkoxy, Aryloxyalkyl, Carboxyalkyl, Carboalkoxy, Alkoxycarbonyl, Carboaralkoxy, Carboxamido, Carboxamidoalkyl, Carbohalogenalkoxy, Phosphono, Phosphonoalkyl, Diaralkoxyphosphono und Diaralkoxyphosphonoalkyl, substituiert sein kann,
mit der Maßgabe, dass mindestens eine der Gruppierungen R_4, R_5, R_6, R_7 und R_8 nicht Hydrido ist,
und mit der weiteren Maßgabe, dass mindestens eine der Gruppierungen R_9, R_{10}, R_{11}, R_{12} und R_{13} nicht Hydrido ist.

2. Verbindung nach Anspruch 1 der Formel M:

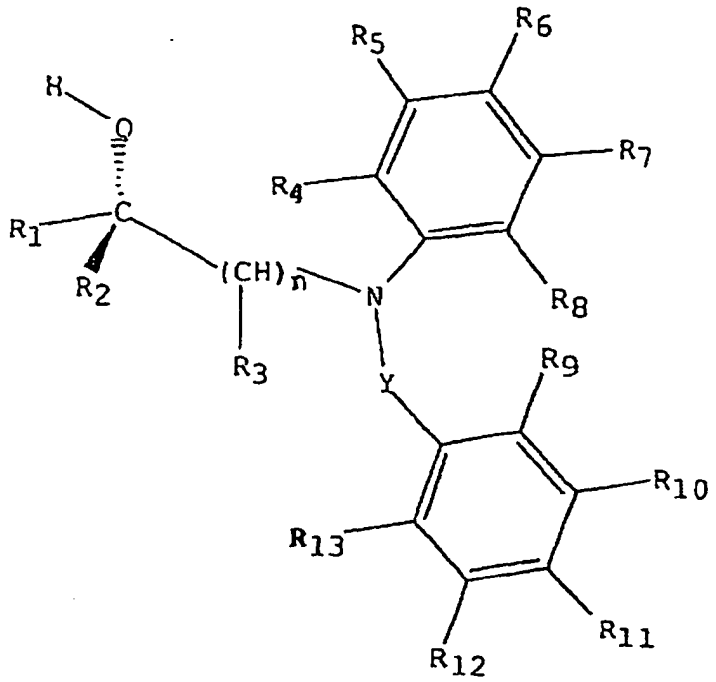


(M)

oder ein pharmazeutisch annehmbares Salz davon, worin
n eine ganze Zahl, ausgewählt aus 1 bis 3, ist;
Y für $-(CH_2)_q-$ steht, wobei q den Wert 1 oder 2 hat;
R_1 für Halogenalkyl steht;
R_2 für Hydrido steht;
R_3 für Hydrido steht,
R_4 , R_8 , R_9 und R_{13} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Halogen, Halogenalkyl und Alkyl, ausgewählt sind,
R_5, R_6, R_7, R_{10}, R_{11} und R_{12} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Heteroaralkoxy, Acylalkyl, Acylalkoxy, Aroylalkoxy, Heterocyclyloxy, Aralkylaryl, Aralkyl, Perhalogenaralkyl, Aralkylsulfonyl, Aralkylsulfonylalkyl, Halogencycloalkyl, Cycloalkylsulfonyl, Cycloalkylsulfonylalkyl, Halogenalkylthio, Alkanoyloxy, Alkoxy, Alkoxyalkyl, Heteroaralkoxy, Cycloalkoxy, Cycloalkoxyalkyl, Cycloalkylalkoxy, Halogencycloalkoxy, Halogencycloalkoxyalkyl, Hydroxy, Amino, Nitro, C_1-C_6-Alkylamino, Alkylthio, Alkylthioalkyl, Arylamino, Aralkylamino, Arylthio, Arylsulfonylalkyl, Alkylsulfonyl, Alkylsulfonylalkyl, Halogenalkylsulfonylalkyl, Alkylsulfonamido, Alkylaminosulfonyl, Amidosulfonyl, Alkylamidosulfonyl, Arylsulfonyl, Alkanoyl, Aroyl, Aralkanoyl, Heteroaralkanoyl, Halo-

genalkanoyl, Alkyl, Cycloalkyl, Cycloalkylalkanoyl, C_3-C_7-Cycloalkylalkyl, Halogen, Halogenalkyl, Halogenalkoxy, Hydroxyhalogenalkyl, Hydroxyaralkyl, Hydroxyalkyl, Halogenalkoxyalkyl, Aryl, Aryloxy, Aralkoxy, Aryloxyalkyl, Heteroaryloxy, Heteroaryloxyalkyl, Carboxyalkyl, Carboalkoxy, Alkoxycarboxamido, Carboalkoxyalkyl, Carboaralkoxy, Carboxamido, Carboxamidoalkyl, Cyano, Carbohalogenalkoxy, Phosphono, Phosphonoalkyl, Diaralkoxyphosphono und Diaralkoxyphosphonoalkyl, ausgewählt sind;
wobei weiterhin, wenn R_7 für Aryloxy oder Aralkoxy steht, das genannte Aryloxy oder Aralkoxy an einer oder mehreren substituierbaren Positionen mit einem oder mehreren Resten, ausgewählt aus Amino, Halogen, Nitro, Alkoxy, Alkyl, Cyano, Cycloalkoxy, Cycloalkyl, Cycloalkylalkoxy, Halogenalkoxy, C_1-C_6-Alkylamino, Halogenalkyl, Alkanoyl und Halogenalkylthio, substituiert sein kann,
mit der Maßgabe, dass mindestens eine der Gruppierungen R_4, R_5, R_6, R_7 und R_8 nicht Hydrido ist,
und mit der weiteren Maßgabe, dass mindestens eine der Gruppierungen R_9, R_{10}, R_{11}, R_{12} und R_{13} nicht Hydrido ist.

3. Verbindung nach Anspruch 2 der Formel M:

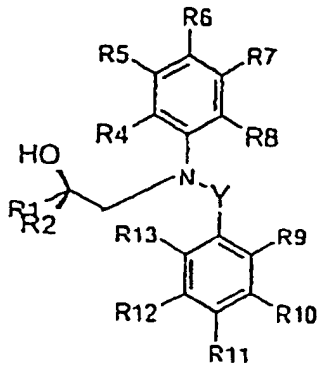


(M)

oder ein pharmazeutisch annehmbares Salz davon, worin
n eine ganze Zahl, ausgewählt aus 1 bis 3, ist;
Y für $-(CH_2)_q-$ steht, wobei q den Wert 1 oder 2 hat;
R_1 für Halogenalkyl steht;
R_2 für Hydrido steht;
R_3 für Hydrido steht,
R_4, R_8, R_9 und R_{13} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Halogen und Halogenalkyl, ausgewählt sind,
R_5, R_6, R_7, R_{10}, R_{11} und R_{12} unabhängig voneinander aus der Gruppe, bestehend aus Hydrido, Heteroaralkoxy, Acylalkyl, Acylalkoxy, Aroylalkoxy, Heterocyclyloxy, Aralkylaryl, Aralkyl, Perhalogenaralkyl, Halogenalkylthio, Alkanoyloxy, Alkoxy, Alkoxyalkyl, Heteroaralkoxy, Cycloalkoxy, Cycloalkoxyalkyl, Cycloalkylalkoxy, Halogencycloalkoxy, Halogencycloalkoxyalkyl, Alkylthio, Alkylthioalkyl, Arylthio, Alkylsulfonyl, Alkylsulfonylalkyl, Halogenalkylsulfonylalkyl, Alkylsulfonamido, Alkylaminosulfonyl, Amidosulfonyl, Alkylamidosulfonyl, Arylsulfonyl, Alkanoyl, Halogenalkanoyl, Alkyl, Cycloalkyl, C_3-C_7-Cycloalkylalkyl, Halogen, Halogenalkyl, Halogenalkoxy, Halogenalkoxyalkyl, Aryl, Aryloxy, Aralkoxy, Aryloxyalkyl, Heteroaryloxy, Heteroaryloxyalkyl, Carboalkoxy, Carboalkoxyalkyl,

Carboaralkoxy und Carbohalogenalkoxy, ausgewählt sind;
wobei weiterhin, wenn R_7 für Aryloxy oder Aralkoxy steht, das genannte Aryloxy oder Aralkoxy an einer oder mehreren substituierbaren Positionen mit einem oder mehreren Resten, ausgewählt aus Amino, Halogen, Nitro, Alkoxy, Alkyl, Cycloalkoxy, Cycloalkyl, Cycloalkylalkoxy, Halogenalkoxy, C_1-C_6-Alkylamino, Halogenalkyl, Alkanoyl und Halogenthio, substituiert sein kann,

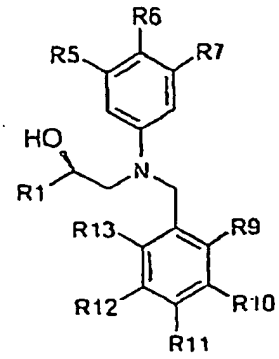
4. Verbindung nach Anspruch 3 der Formel "D"



Formel "D"

worin Y für $-CH_2-$ steht;
worin R^1 für Halogenalkyl steht;
worin R^2 für Hydrido steht;
worin R^4 und R^8 für Hydrido stehen;
worin R^5 und R^6 aus Hydrido und Alkoxy ausgewählt sind;
worin R^7 aus Aryloxy, Arylalkoxy, 5,6,7,8-Tetrahydronaphth-2-yloxy, Alkoxy, Cycloalkoxy, Cycloalkylalkoxy und Halogen ausgewählt ist;
wobei die genannten Aryloxy- und Arylalkoxy-Gruppen in R^7 an einer oder mehreren substituierbaren Positionen mit einem oder mehreren Resten, ausgewählt aus Halogen, Alkyl, Alkoxy, Halogenalkoxy und Halogenalkyl, substituiert sein können;
worin R^9 aus Hydrido, Halogen und Halogenalkyl ausgewählt ist;
worin R^{10} aus Halogenalkoxy, Halogenalkyl und Halogenalkylthio ausgewählt ist;
worin R^{11} aus Hydrido, Halogen und Halogenalkyl ausgewählt ist;
worin R^{12} aus Hydrido und Halogenalkyl ausgewählt ist;
worin R^{13} aus Hydrido, Halogen und Halogenalkyl ausgewählt ist.

5. Verbindung nach Anspruch 4 der Formel "C"



Formel "C"

worin R^1 aus Trifluormethyl und Chlormethyl ausgewählt ist;
worin R^5 und R^6 aus Hydrido und Methoxy ausgewählt sind;
worin R^7 aus Phenyloxy, Benzyloxy, 5,6,7,8-Tetrahydronaphth-2-yloxy, Isopropoxy, Cyclopentoxy, Brom, Cyclohexylmethoxy und Methoxy ausgewählt ist;
worin die genannten Phenyloxy- und Benzyloxygruppen in R^7 an einer oder mehreren substituierbaren Positionen mit einem oder mehreren Resten, ausgewählt aus Chlor, Ethyl, Trifluormethoxy, Brom, Fluor, Methyl, Isopropyl, Trifluormethyl, Isopropoxy und tert.-Butyl, substituiert sein können;
worin R^9 aus Hydrido, Fluor und Trifluormethyl ausgewählt ist,
worin R^{10} aus 1,1,2,2-Tetrafluorethoxy, Trifluormethoxy, Pentafluorethyl, Trifluormethyl und Trifluormethylthio ausgewählt ist;
worin R^{11} aus Hydrido, Trifluormethyl und Fluor ausgewählt ist;
worin R^{12} aus Hydrido und Trifluormethyl ausgewählt ist;
worin R^{13} aus Hydrido, Fluor und Trifluormethyl ausgewählt ist.

6. Verbindung nach Anspruch 5 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung aus der Gruppe, bestehend aus:

(2R)-3-[[3-(3-Trifluormethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(3-Isopropylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(4-Methylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(2-Brom-5-fluorphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(3-Ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(Phenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)-phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[[3-(1,1,2,2-Tetrafluorethoxy)phenyl]methyl][3-[[3-(3-trifluormethoxy)phenyl]methoxy]phenyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[[3-(1,1,2,2-Tetrafluorethoxy)phenyl]methyl][3-[[3-(trifluormethyl)phenyl]methoxy]phenyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[[3-(1,1,2,2-Tetrafluorethoxy)phenyl]methyl][3-[[3,5-difluorphenyl]methoxy]phenyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-Isopropoxyphenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[(3-(4-Chlor-3-ethylphenoxy)phenyl][[3-(pentafluorethyl)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[2-fluor-5-(trifluormethyl)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[2-fluor-4-(trifluormethyl)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol;

(2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[3-(trifluormethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-pro-

panol;

(2R)-3-[[3-(3-(Trifluormethoxy)phenoxy)phenyl][[3-(trifluormethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol und

(2R)-3-[[3-(4-Methylphenoxy)phenyl][[3-(trifluormethoxy)-phenyl]methyl]amino]-1,1,1-trifluor-2-propanol.

7. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

8. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[(3-Phenoxyphenyl)[[3-(1,1,2,2-tetrafluorethoxy)-phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

9. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(4-Methylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

10. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(3-Isopropylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

11. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(3-Ethylphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

12. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(3-Trifluormethoxyphenoxy)phenyl][[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

13. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[3-(4-Chlor-3-ethylphenoxy)phenyl][[3-(trifluormethoxy)phenyl]methyl]amino]-1,1,1-trifluor-2-propanol ist.

14. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[[3-(1,1,2,2-tetrafluorethoxy)phenyl]methyl][3-[[3-(trifluormethyl)phenyl]methoxy]phenyl]amino]-1,1,1-trifluor-2-propanol ist.

15. Verbindung nach Anspruch 6 oder ein pharmazeutisch annehmbares Salz davon, wobei die genannte Verbindung (2R)-3-[[[3-(1,1,2,2-Tetrafluorethoxy)phenyl]methyl][3-[[3-(trifluormethoxy)phenyl]methoxy]phenyl]amino]-1,1,1-trifluor-2-propanol ist.

16. Pharmazeutisches Präparat, umfassend eine therapeutisch wirksame Menge einer Verbindung nach Anspruch 1 oder eines pharmazeutisch annehmbaren Salzes davon zusammen mit einem pharmazeutisch annehmbaren Träger.

17. Verwendung der Verbindung nach Anspruch 1 oder eines pharmazeutisch annehmbaren Salzes davon für die Herstellung eines Medikaments zur Behandlung oder Prophylaxe einer durch CETP vermittelten Störung in einem Menschen.

18. Verwendung nach Anspruch 17, wobei die Behandlung der durch CETP vermittelten Störung eine Erkrankung der Coronararterien ist.

19. Verwendung nach Anspruch 17, wobei die Prophylaxe der durch CETP vermittelten Störung eine Erkrankung der Coronararterien ist.

20. Verwendung nach Anspruch 17, wobei die Prophylaxe einer durch CETP vermittelten Störung die Prophylaxe eines Schlaganfalls (CVA; "cerebral vascular accident") ist.

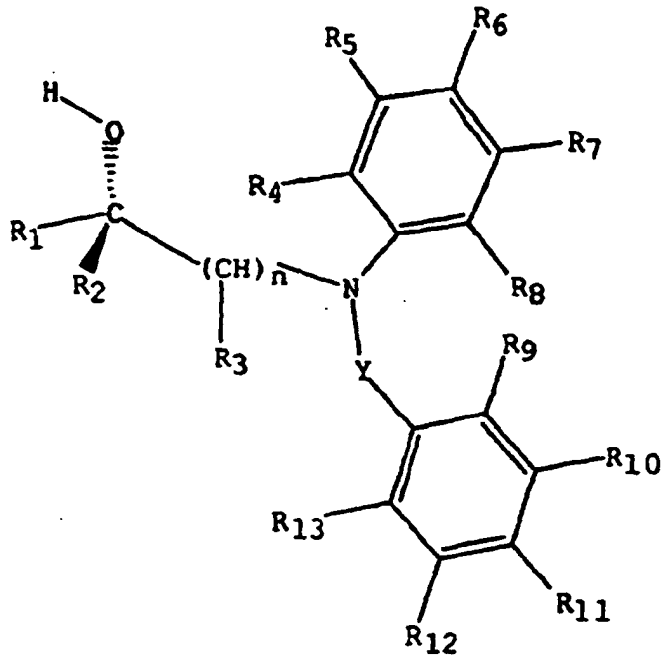
21. Verwendung nach Anspruch 17, wobei die Behandlung der durch CETP vermittelten Störung die Behandlung einer

Dyslipidämie ist.

22. Verwendung nach Anspruch 17, wobei die Prophylaxe der durch CETP vermittelten Störung die Behandlung einer Dyslipidämie ist.

Revendications

1. Composé de formule M :



(M)

ou un sel pharmaceutiquement acceptable de celui-ci, dans laquelle ;
n est choisi parmi les nombres entiers 1, 2, 3 et 4 ;
Y est $-(CH_2)_q-$ dans lequel q vaut 1 ou 2 ;
R_1 est un groupe halogénoalkyle ;
R_2 est un atome d'hydrogène ;
R_3 est un atome d'hydrogène ;
R_4, R_8, R_9 et R_{13} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, halogène, halogénoalkyle et alkyle ;
R_5, R_6, R_7, R_{10}, R_{11} et R_{12} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, carboxy, hétéroaralkylthio, hétéroaralcoxy, cycloalkylamino, acylalkyle, acylalcoxy, aroylalcoxy, hétérocyclyloxy, aralkylaryle, aralkyle, aralcényle, aralcynyle, hétérocyclyle, perhalogénoaralkyle, aralkylsulfonyle, aralkylsulfonylalkyle, aralkylsulfinyle, aralkylsulfinylalkyle, halogénocycloalkyle, halogénocycloalcényle, cycloalkylsulfinyle, cycloalkylsulfinylalkyle, cycloalkylsulfonyle, cycloalkylsufonylalkyle, hétéroarylamino, N-hétéroarylamino-N-alkylamino, hétéroarylaminoalkyle, halogénoalkylthio, alcanoyloxy, alcoxy, alcoxyalkyle, hétéroaralcoxy, cycloalcoxy, cycloalcényloxy, cycloalcoxyalkyle, cycloalkylalcoxy, cycloalcényloxyalkyle, halogénocycloalcoxy, halogénocycloalcoxyalkyle, halogénocycloalcényloxy, halogénocycloalcényloxyalkyle, hydroxy, amino, thio, nitro, (alkyle en C_1-C_6) amino, alkylthio, alkylthioalkyle, arylamino, aralkylamino, arylthio, arylthioalkyle, hétéroaralcoxyalkyle, alkylsulfinyle, alkylsulfinylalkyle, arylsulfinylalkyle, arylsulfonylalkyle, hétéroarylsulfinylalkyle, hétéroarylsulfonylalkyle, alkylsulfonyle, alkylsulfonylalkyle, halogénosulfinylalkyle, halogénoalkylsulfonylalkyle, alkylsulfonamido, alkylaminosulfonyle, amidosulfonyle, alkylamidosulfonyle, arylamidosulfonyle, arylsulfonamido, alkylarylamidosulfonyle, arylsulfinyle, arylsulfonyle, hétéroarylthio, hétéroarylsulfinyle, hétéroarylsulfonyle, hétérocyclylsulfonyle, hétérocyclylthio, alcanoyle, alcénoyle, aroyle, hétéroaroyle, aralcanoyle, hétéroaralcanoyle, halogénoalcanoyle, alkyle, alcé-

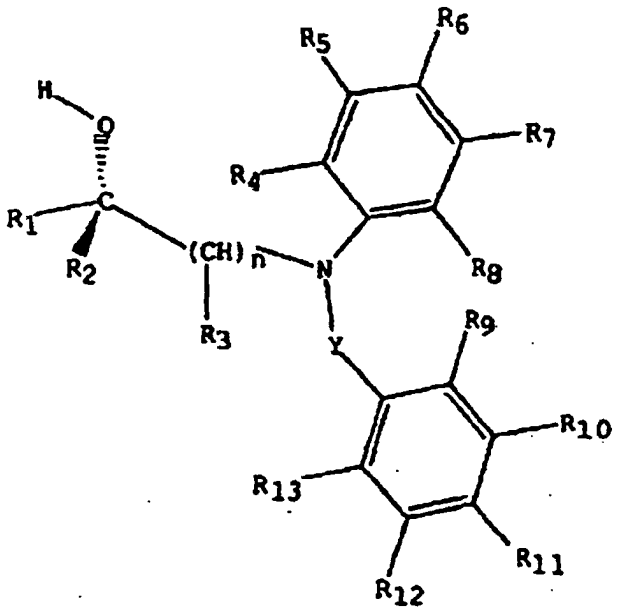
nyle, alcynylé, alcényloxy, alcényloxyalkyle, cycloalkyle, cycloalkylalcanoyle, cycloalcényle, (cycloalkyle en C_3-C_7) alkyle, (cycloalcényle en C_3-C_7)alkyle, halogène, halogénoalkyle, halogénoalcényle, halogénoalcoxy, hydroxyhalogénoalkyle, hydroxyaralkyle, hydroxyalkyle, hydroxyhétéroaralkyle, halogénoalcoxyalkyle, aryle, hétéroaralcynyle, aryloxy, aralcoxy, aryloxyalkyle, hétérocyclyle saturé, hétérocyclyle partiellement saturé, hétéroaryle, hétéroaryloxy, hétéroaryloxyalkyle, hétéroaralkyle, arylalcényle, hétéroarylalcényle, carboxyalkyle, carboalcoxy, alcoxycarboxamido, alkylamidocarbonylamido, arylamidocarbonylamido, carboalcoxyalkyle, carboalcoxyalcényle, carboaralcoxy, carboxamido, carboxamidoalkyle, cyano, carbohalogénoalcoxy, phosphono, phosphonoalkyle, diaralcoxyphosphono et diaralcoxyphosphonoalkyle ;

en outre, dans laquelle lorsque R_7 est un groupe aryloxy ou aralcoxy, ledit groupe aryloxy ou aralcoxy peut être substitué en une ou plusieurs positions substituables par un ou plusieurs radicaux choisis parmi les groupes amino, halogène, nitro, alcoxy, alkyle, cyano, cycloalcoxy, cycloalkyle, cycloalkylalcoxy, halogénoalcoxy, (alkyle en C_1-C_6)amino, halogénoalkyle, alcanoyle, halogénoalkylthio, perhalogénoaralkyle, aralkylsulforiyle, aralkylsulfonylalkyle, halogénocycloalkyle, halogénocycloalcényle, halogénoalkylthio, alcanoyloxy, alcoxy, alcoxyalkyle, halogénoalcoxyalkyle, cycloalcoxy, cycloalcoxyalkyle, cycloalkylalcoxy, hydroxy, thio, alkylthio, alkylthioalkyle, arylamino, aralkylamino, arylthio, arylthioalkyle, alkylsulfonyle, alkylsulfonylalkyle, halogénoalkylsulfonylalkyle, alkylsulfonamido, alkylaminosulfonyle, amidosulfonyle, monoalkylamidosulfonyle, dialkylamidosulfonyle, arylsulfonyle, alcénoyle, aroyle, aralcanoyle, halogénoalcanoyle, alcényle, alcynyle, alcényloxy, alcényloxyalkyle, cycloalkylalcanoyle, (cycloalkyle en C_3-C_7) alkyle, halogénoalcényle, hydroxyhalogénoalkyle, hydroxyaralkyle, hydroxyalkyle, halogénoalcoxyalkyle, aryle, aralkyle, aryloxy, aralcoxy, aryloxyalkyle, carboxyalkyle, carboalcoxy, alcoxycarbonyle, carboaralcoxy, carboxamide, carboxamidoalkyle, carbohalogénoalcoxy, phosphono, phosphonoalkyle, diaralcoxyphosphono etdiaralcoxyphosphonoalkyle,

à condition qu'au moins un des groupes R_4, R_5, R_6, R_7 et R_8 ne soit pas un atome d'hydrogène,

et à une autre condition qu'au moins un des groupes R_9, R_{10}, R_{11}, R_{12} et R_{13} ne soit pas un atome d'hydrogène.

2. Composé selon la revendication 1 de formule M :



(M)

ou un sel pharmaceutiquement acceptable de celui-ci, dans laquelle ;

n est un nombre entier valant de 1, 2 à 3 ;

Y est $-(CH_2)_q-$ dans lequel q vaut 1 ou 2 ;

R_1 est un groupe halogénoalkyle ;

R_2 est un atome d'hydrogène ;

R_3 est un atome d'hydrogène ;

R_4, R_8, R_9 et R_{13} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, halogène et halogénoalkyle ;

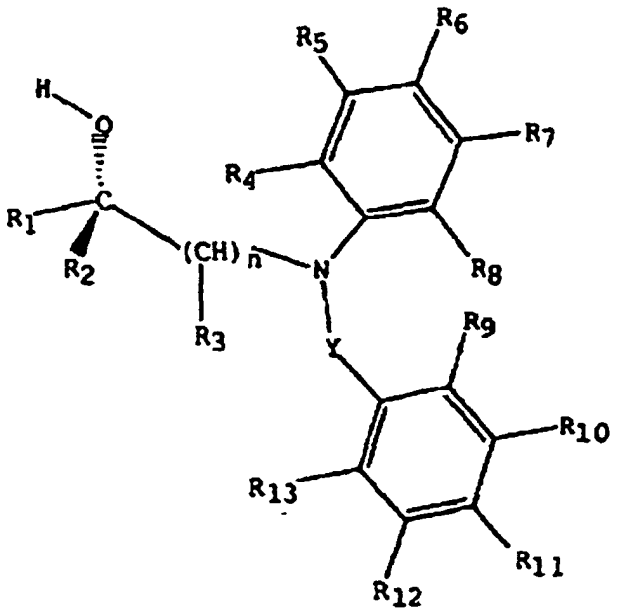
R_5, R_6, R_7, R_{10}, R_{11} et R_{12} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, hétéroaralcoxy, acylalkyle, acylalcoxy, aroylalcoxy, hétérocyclyloxy, aralkylaryle, aralkyle, perhalogénoaralkyle, aralkylsulfonyle, aralkylsulfonylalkyle, halogénocycloalkyle, cycloalkylsulfonyle, cycloalkylsufonylalkyle, halogénoalkylthio, alcanoyloxy, alcoxy, alcoxyalkyle, hétéroaralcoxy, cycloalcoxy, cycloalcoxyalkyle, cycloalkylalcoxy, halogénocycloalcoxy, halogénocycloalcoxyalkyle, hydroxy, amino, nitro, (alkyle en C_1-C_6)amino, alkylthio, alkylthioalkyle, arylamino, aralkylamino, arylthio, arylsulfonylalkyle, alkylsulfonyle, alkylsulfonylalkyle, halogénoalkylsulfonylalkyle, alkylsulfonamido, alkylaminosulfonyle, amidosulfonyle, alkylamidosulfonyle, arylsulfonyle, alcanoyle, aroyle, aralcanoyle, hétéroaralcanoyle, halogénoalcanoyle, alkyle, cycloalkyle, cycloalkylalcanoyle, (cycloalkyle en C_3-C_7)alkyle, halogène, halogénoalkyle, halogénoalcoxy, hydroxyhalogénoalkyle, hydroxyaralkyle, hydroxyalkyle, halogénoalcoxyalkyle, aryle, aryloxy, aralcoxy, aryloxyalkyle, hétéroaryloxy, hétéroaryloxyalkyle, carboxyalkyle, carboalcoxy, alcoxycarboxamido, carboalcoxyalkyle, carboaralcoxy, carboxamido, carboxamidoalkyle, cyano, carbohalogénoalcoxy, phosphono, phosphonoalkyle, diaralcoxyphosphono et diaralcoxyphosphonoalkyle ;

en outre, dans laquelle lorsque R_7 est un groupe aryloxy ou aralcoxy, ledit groupe aryloxy ou aralcoxy peut être substitué en une ou plusieurs positions substituables par un ou plusieurs radicaux choisis parmi les groupes amino, halogène, nitro, alcoxy, alkyle, cyano, cycloalcoxy, cycloalkyle, cycloalkylalcoxy, halogénoalcoxy, (alkyle en C_1-C_6)amino, halogénoalkyle, alcanoyle et halogénoalkylthio ;

à condition qu'au moins un des groupes R_4, R_5, R_6, R_7 et R_8 ne soit pas un atome d'hydrogène,

et à une autre condition qu'au moins un des groupes R_9, R_{10}, R_{11}, R_{12} et R_{13} ne soit pas un atome d'hydrogène.

3. Composé selon la revendication 2 de formule M :



(M)

ou un sel pharmaceutiquement acceptable de celui-ci, dans laquelle ;

n est un nombre entier valant de 1, 2 à 3 ;

Y est -$(CH_2)_q$- dans lequel q vaut 1 ou 2 ;

R_1 est un groupe halogénoalkyle ;

R_2 est un atome d'hydrogène ;

R_3 est un atome d'hydrogène ;

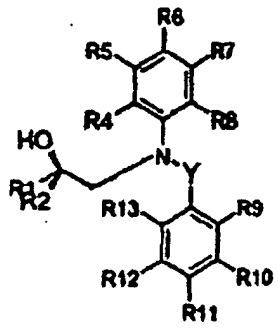
R_4, R_8, R_9 et R_{13} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, halogène et halogénoalkyle ;

R_5, R_6, R_7, R_{10}, R_{11} et R_{12} sont indépendamment choisis dans le groupe constitué des groupes hydrogène, hétéroaralcoxy, acylalkyle, acylalcoxy, aroylalcoxy, hétérocyclyloxy, aralkylaryle, aralkyle, perhalogénoaralkyle,

halogénoalkylthio, alcanoyloxy, alcoxy, alcoxyalkyle, hétéroaralcoxy, cycloalcoxy, cycloalcoxyalkyle, cycloalkylalcoxy, halogénocycloalcoxy, halogénocycloalcoxyalkyle, alkylthio, alkylthioalkyle, arylthio, alkylsulfonyle, alkylsulfonylalkyle, halogénoalkylsulfonylalkyle, alkylsulfonamido, alkylaminosulfonyle, amidosulfonyle, alkylamidosulfonyle, arylsulfonyle, alcanoyle, halogénoalcanoyle, alkyle, cycloalkyle, (cycloalkyle en C_3-C_7)alkyle, halogène, halogénoalkyle, halogénoalcoxy, halogénoalcoxyalkyle, aryle, aryloxy, aralcoxy, aryloxyalkyle, hétéroaryloxy, hétéroaryloxyalkyle, carboalcoxy, carboalcoxyalkyle, carboaralcoxy et carbohalogénoalcoxy ;

en outre, dans laquelle lorsque R_7 est un groupe aryloxy ou aralcoxy, ledit groupe aryloxy ou aralcoxy peut être substitué en une ou plusieurs positions substituables par un ou plusieurs radicaux choisis parmi les groupes amino, halogène, nitro, alcoxy, alkyle, cycloalcoxy, cycloalkyle, cycloalkylalcoxy, halogénoalcoxy, (alkyle en C_1-C_6) amino, halogénoalkyle, alcanoyle et halogénoalkylthio.

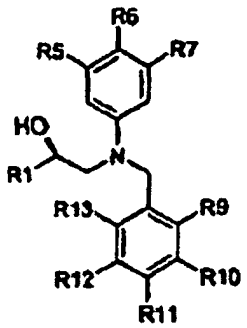
4. Composé selon la revendication 3 de formule « D »



Formule « D »

dans laquelle Y est -CH_2- ;
dans laquelle R^1 est un groupe halogénoalkyle ;
dans laquelle R^2 est un atome d'hydrogène ;
dans laquelle R^4 et R^8 sont des atomes d'hydrogène ;
dans laquelle R^5 et R^6 sont choisis parmi les groupes hydrogène et alcoxy ;
dans laquelle R^7 est choisi parmi les groupes aryloxy, arylalcoxy, 5,6,7,8-tétrahydronapht-2-yloxy, alcoxy, cycloalcoxy, cycloalkylalcoxy et halogène ;
dans laquelle lesdits groupes aryloxy et arylalcoxy de R^7 peuvent être substitués en une ou plusieurs positions substituables par un ou plusieurs radicaux choisis parmi les groupes halogène, alkyle, alcoxy, halogénoalcoxy et halogénoalkyle ;
dans laquelle R^9 est choisi parmi les groupes hydrogène, halogène et halogénoalkyle ;
dans laquelle R^{10} est choisi parmi les groupes halogénoalcoxy, halogénoalkyle et halogénoalkylthio ;
dans laquelle R^{11} est choisi parmi les groupes hydrogène, halogène et halogénoalkyle ;
dans laquelle R^{12} est choisi parmi les groupes hydrogène et halogénoalkyle ;
dans laquelle R^{13} est choisi parmi les groupes hydrogène, halogène et halogénoalkyle.

5. Composé selon la revendication 4 de formule « C »



Formule « C »

dans laquelle R^1 est choisi parmi les groupes trifluorométhyle et chlorométhyle ;
dans laquelle R^5 et R^6 sont choisis parmi les groupes hydrogène et méthoxy ;
dans laquelle R^7 est choisi parmi les groupes phényloxy, benzyloxy, 5,6,7,8-tétrahydronapht-2-yloxy, isopropoxy, cyclopentoxy, brome, cyclohexylméthyle et méthoxy ;
dans laquelle lesdits groupes phényloxy et benzyloxy de R^7 peuvent être substitués en une ou plusieurs positions substituables par un ou plusieurs radicaux choisis parmi les groupes chlore, éthyle, trifluorométhoxy, brome, fluor, méthyle, isopropyle, trifluorométhyle, isopropoxy et tert-butyle ;
dans laquelle R^9 est choisi parmi les groupes hydrogène, fluor et trifluorométhyle ;
dans laquelle R^{10} est choisi parmi les groupes 1,1,2,2-tétrafluoroéthoxy, trifluorométhoxy, pentafluoroéthyle, trifluorométhyle et trifluorométhylthio ;
dans laquelle R^{11} est choisi parmi les groupes hydrogène, trifluorométhyle et fluor ;
dans laquelle R^{12} est choisi parmi les groupes hydrogène et trifluorométhyle ;
dans laquelle R^{13} est choisi parmi les groupes hydrogène, fluor et trifluorométhyle.

6. Composé selon la revendication 5, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est choisi dans le groupe constitué de :

(2R)-3-[[3-(3-trifluorométhoxyphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(3-isopropylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-méthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(2-bromo-5-fluorophénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]mêthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(3-éthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(phénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[[3-(1,1,2,2-tétrafluoroéthoxy)phényl]méthyl][3-[[3-(trifluorométhoxy)-phényl]méthoxy]phényl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[[3-(1,1,2,2-tétrafluoroéthoxy)phényl]méthyl][3-[[3-(trifluorométhyl)-phényl]méthoxy]phényl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[[3-(1,1,2,2-tétrafluoroéthoxy)phényl]méthyl][3-[[3,5-difluorophényl]méthoxy]phényl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-isopropoxyphényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[3-(pentafluoroéthyl)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;

(2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[2-fluoro-5-(trifluorométhyl)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[2-fluoro-4-(trifluorométhyl)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[3-(trifluorométhoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(3-(trifluorométhoxy)phénoxy)phényl][[3-(trifluorométhoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol ;
(2R)-3-[[3-(4-méthylphénoxy)phényl][[3-(trifluorométhoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

7. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

8. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[(3-phénoxyphényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

9. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R) -3-[[3-(4-méthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

10. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[3-(3-isopropylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

11. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[3-(3-éthylphénoxy)phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

12. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[3-(3-trifluorométhoxyphénoxy)-phényl][[3-(1,1,2,2-tétrafluoroéthoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

13. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[3-(4-chloro-3-éthylphénoxy)phényl][[3-(trifluorométhoxy)-phényl]méthyl]amino]-1,1,1-trifluoro-2-propanol.

14. Composé selon la revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[[3-(1,1,2,2-tétrafluoroéthoxy)phényl]-méthyl][3-[[3-(trifluorométhyl)-phényl]méthoxy]phényl] amino]-1,1,1-trifluoro-2-propanol.

15. Composé selon 1a revendication 6, ou un sel pharmaceutiquement acceptable de celui-ci, dans lequel ledit composé est le (2R)-3-[[[3-(1,1,2,2-tétrafluoroéthoxy)phényl]-méthyl][3-[[3-(trifluorométhoxy)-phényl]méthoxy]phényl] amino]-1,1,1-trifluoro-2-propanol.

16. Composition pharmaceutique comprenant une quantité thérapeutiquement efficace d'un composé selon la revendication 1 ou d'un sel pharmaceutiquement acceptable de celui-ci, avec un vecteur pharmaceutiquement acceptable.

17. Utilisation d'un composé selon la revendication 1 ou d'un sel pharmaceutiquement acceptable de celui-ci pour la fabrication d'un médicament destiné au traitement ou à la prévention d'un trouble médié par la CETP chez un sujet.

18. Utilisation selon la revendication 17, dans laquelle le traitement d'un trouble médié par la CETP est le traitement d'une maladie coronarienne.

19. Utilisation selon la revendication 17, dans laquelle la prévention d'un trouble médié par la CETP est la prévention d'une maladie coronarienne.

20. Utilisation selon la revendication 17, dans laquelle la prévention d'un trouble médié par la CETP est la prévention d'un accident vasculaire cérébral (AVC).

21. Utilisation selon la revendication 17, dans laquelle le traitement d'un trouble médié par la CETP est le traitement d'une dyslipidémie.

22. Utilisation selon la revendication 17, dans laquelle la prévention d'un trouble médié par la CETP est la prévention d'une dyslipidémie.